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Original Article

Effect of Intravitreal Injection of Bevacizumab on Intraocular Pressure in Relation to Different Ocular Axial Lengths

Authors

Mohsin Javaid[1]

Asad Aslam Khan[2]

Haroon Tayyab[3]

Ch Nasir Ahmed[4]

For Authors' Affiliation See Last Page of Article

Correspondence Author:
Dr. Rana Muhammad Mohsin Javaid
VR Fellow King Edward Medical University, Lahore.
Email: lmdc99@hotmail.com

Purpose: To determine the effect of intravitreal injection of bevacizumab on intraocular pressure in relation to different ocular axial lengths.

Study Design: Quasi experimental study.

Place and Duration of Study: Eye unit-III, Institute Of Ophthalmology, King Edward Medical University, Mayo Hospital Lahore. The study was conducted from October 2017 to March 2018.

Material and Methods: A total of 100 patients who presented with wet AMD, diabetic macular edema, retinal vein occlusion related macular edema and having IOP <21 mm Hg without medication and eligible for their first intravitreal bevacizumab injection were included in the study. Axial length was measured preoperatively using ultrasound biometer. The same surgeon performed all intravitreal bevacizumab injections by using 30-gauge needles penetrating the inferotemporal pars plana at 3.5 mm from the limbus through the displaced conjunctiva. Intraocular pressure was measured in the clinostatic position before and immediately after the injection (within 1 min), and also 15 and 30 minutes later using Perkins Tonometer.

Results: Mean axial length measured was 22.60±1.64 mm. Before injection mean IOP was 15.57±2.24. After injection rise in IOP at 1, 15 and 30 minutes was 29.09±11.35, 20.79±4.22 and 18.14±3.01mmHg respectively. Strong inverse correlation was observed between axial length and IOP after injection at 1 (r: -0.596, p-value=0.000), 15 (r: -0.496, p-value=0.000) and 30 minutes(r: -0.482, p-value=0.000).
Conclusion: The results of this study showed a remarkable transient increase in IOP after intravitreal injectionof bevacizumab. A significant inverse correlation was observed between axial length and IOP after intravitreal injection showing a meaningful association between these two parameters.

Keywords: Intravitreal injection, Bevacizumab, Intraocular pressure, Ocular, Axial lengths.

Introduction:

The use of Intravitreal injections is very common nowadays for treating many retinal diseases, and injection of bevacizumab, which is a humanized monoclonal anti-VEGF antibody is the most frequently used therapeutic modality for treating macular edema secondary to retinal vein occlusion, diabetic retinopathy, and age-related macular degeneration. It is being observed that the use of Intravitreal bevacizumab injection is increasing in retinal clinics due to its efficacy and cost-effectiveness. Despite its frequent use intravitreal injection have several complications like vitreous hemorrhage, retinal detachment, endophthalmitis, intraocular inflammation, and persistent IOP elevation.

An increase in intraocular fluid volume directly relates to the short term elevation of IOP after anti-VEGF. Other latent variables influencing IOP rise comprise scleral thickness, axial length, ocular outflow facility and scleral rigidity.

After intravitreal injections, the cause of sustained elevation of intraocular pressure remained unknown. Several theories have been proposed, including a permanent decrease in outflow facility dueto repeated IOP spikes with each injection and subsequent damage to the trabecular meshwork, direct pharmacological toxicity, and chronic trabeculitis.

Short axial length is considered as a possible risk factor for immediate IOP rise after the intravitreal injection. Intraocular volume is smaller in eyes with shorter axial length, thus even the same volume may induce more IOP rise than those with longer axial length.

Andrea Cacciamani in his study showed a strong inverse correlation between the axial length and intraocular pressure rise after both 1 and 15 min after the injection. Hollands et al. used 0.05 ml of bevacizumab in his study and evaluated the changes in IOP 2, 5 and 30 min after injection. As per his findings, 10 % of subjects may experience an IOP rise>50 mmHg. Gismondi in his study reported that eyes with shorter axial length had higher IOP immediately after the Intravitreal injection of ranibizumab. Based on these finding axial length measurement can be used as a good indicator to predict a possible increase in IOP after intravitreal bevacizumab.

A recent study by H.S. Trehan reported that intravitreal injection of bevacizumab does not lead to changes in the intraocular pressure or anterior chamber depth that can lead to ocular damage in the short term.

The rationale for this study is evident from the above mentioned studies where patients undergoing intravitreal injection of bevacizumab can be exposed to intraocular pressure increases correlated to ocular axial length. However, some studies have shown that intravitreal injection of bevacizumab does not lead to changes in the intraocular pressure or anterior chamber depth which may lead to ocular damage in the short term. This shows controversy regarding the effect of axial length on IOP after intravitreal injection of bevacizumab. To clear this, we planned to do this study so that the simple measurement of ocular axial length in each patient before the first intravitreal bevacizumab could provide useful information regarding the expected increase in IOP.

Objective:

To determine the effect of intravitreal injection of bevacizumab on intraocular pressure in relation to different ocular axial lengths.

Operational Definitions:

Intraocular pressure:

IOP was measured with Perkins's handheld applanation tonometer in supine position just before and immediately after the injection at 1, 15 and 30 minutes.

Axial Length:

Axial length measurements were taken with an ultrasound biometer and were reported as the average of three reliable measurements.

Material & Methods

This was a quasi experimental study conducted at Eye unit-III, Institute Of Ophthalmology, King Edward Medical University, Mayo Hospital Lahore.The study was completed in 06 months from October 2017 to March 2018.

A sample size of 100 patients was taken in the study. Sample selection was done through a nonprobability purposive sampling technique.The inclusion criterion for sample selection was based on the following conditions: Patients of wet AMD eligible for the first Intravitreal bevacizumab, diabetic macular edema, retinal vein occlusion and patients with IOP <21 mm Hg without medication. Exclusion criteria for patients were: use of IOP-lowering agents, baseline IOP >22 mm Hg, history of ocular surgery, laser treatment, family history or diagnosis of Glaucoma and patients with previous intravitreal injection were excluded from the study.

Data Collection:

After getting the approval from the Ethical board 100 patients were selected from OPD of Eye Unit-III. Axial length was measured preoperatively using ultrasound biometer and reported as the average of three reliable measurements. All intravitreal bevacizumab injections were performed by the same surgeon by using a 30-gauge needle penetrating the inferotemporal pars plana at 3.5 mm from the limbus through the displaced conjunctiva. Intraocular pressure was

measured in the clinostatic position before and immediately after the injection (within 1 min), 15 and 30 minutes later using Perkins Tonometer. IOP was reported as the average of three reliable measurements.

Statistical Analysis:

Data entry and analysis was done by using SPSS 21. Quantitative variables (Age, IOP & Axial length) were presented by using mean±SD. Qualitative variables were presented by using frequency and percentages. The correlation coefficient was calculated to see the interdependency of IOP and axial length at different time intervals. One way repeated measure ANOVA/Friedman ANOVA was applied to see the IOP at different time points. p-value < 0.05 was taken as significant.

Results:

In this study, the mean age of patients was 57.93±7.83 years. The minimum and maximum age of patients in this study was 45 and 77 years respectively. Among patients 49(49%) were males and 51(51%) were females. The mean axial length measured was 22.60±1.64 mm. Before injection mean IOP was 15.57±2.24. One minute after injection mean IOP increased to 29.09±11.35 mmHg. Fifteen minutes after injection mean IOP decreased to 20.79±4.22 and after thirty minutes mean IOP decreased to 18.14±3.01mmHg.(Table-1) Strong inverse correlation was observed between axial length and IOP after injection at 1minute (r= -0.596, p-value=0.000) and moderate inverse correlation was observed at 15 minute (r= -0.496, p-value=0.000) and 30 minutes (r= -0.482, p-value=0.000) respectively. (Table-2)

Table-1: Descriptive statistics for IOP before &after injection

	IOP Before Injection	IOP after Injection		
		1 Minute	15 Minutes	30 Minutes
n	100	100	100	100
Mean	15.57	29.09	20.79	18.14
SD	2.24	11.35	4.22	3.01
Minimum	11	18	15	14
Maximum	20	44	27	22

Table-2: Correlation between axial length and IOP after injection

	After Injection (IOP)		
	1 Minute	15 Minutes	30 Minutes
n	100	100	100
Axial length (mm): r	-0.596	-0.496	-0.482
p-value	0.000	0.000	0.000

Figure-1: Correlation between Axial length & IOP after 1 min of injection

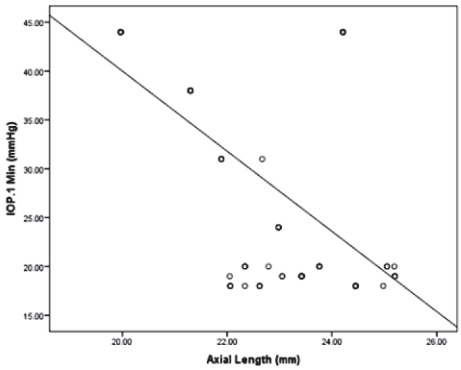


Figure-2: Correlation between Axial length & IOP after 15 min of injection

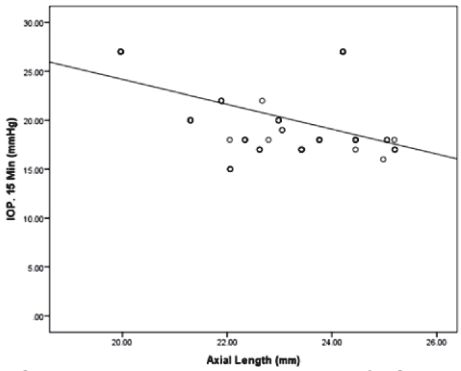
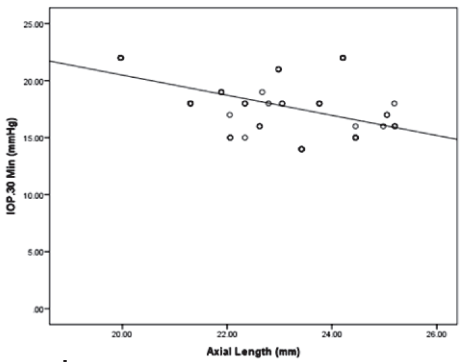


Figure-3: Correlation between Axial length & IOP after 30 min of injection



Discussion:

The use of intravitreal anti-VEGF agents has gained immense importance for treating certainvitreoretinal pathologies worldwide. According to recent evidence rapid and sustained increase in IOP associated with anti-VEGF intravitreal injection therapy is of core concern for the vitreoretinal specialist. In this study, we observed the immediate rise in IOP in patients undergoing intravitreal injectionof bevacizumab. IOP was noted at 1 minute, 15 minutes and 30

minutes after the injection. Before injection mean IOP was 15.57±2.24 mmHg. At 1 minute and 15 minutes after injection mean IOP increased to 29.09±11.35 and 20.79±4.22 and at 30 minutes it was 18.14±3.01. In this study, it was also observed that IOP reached normal value within 30 minutes time span. These findings are consistent with the previous studies.

Altan Goktas in his study showed that after 5 minutes the IOP increased to 24.8 ± 9.5 (13–46) mmHg and within 30 minutes IOP decreased to 24.8 ± 9.5 (13–46) mmHg. Falkenstein et al. in his study reported mean IOP at 3 and 10 minutes after the injection was 21.1 ± 4.76 and 9.39 ± 5.92 with a spontaneous decrease of IOP after 30 minutes of injection.

Andrea Cacciamani in his study reported that about 75% of the variation in IOP changes after the injection is linked with axial length. The author also reported that each mm of shorter axial length can cause a change of 5 mmHg in IOP. Mean IOP change in the study after 1 minuteand 10 minutes after injection was 21.92 ±6.95 mmHg and 6.24 ± 3.77 mmHg.

Studies have reported a strong inverse correlation between axial length (ocular anatomical features particularly eye size) and IOP after injection.

Cacciamani et al in his study reported strong inverse correlation between axial length and IOP to increase at 1 and 15 minutes after injection i.e. (R2 = 0.752, p<0.001) and 15 min (R2 = 0.559, p<0.001). A recent study by Sumayya Khan also reported the similar findings showing very strong inverse correlation between axial length and rise in IOP after 1 minute of injection. Pearson correlation (r.) = -0.914 (p-value <0.001) with R2 = 0.835. Similar findings were seen in this study that a strong inverse correlation between axial length and rise in IOP at 1, 15 ad 30 minutes after injection.However, AltanGoktas in his study reported no inverse correlation between IOP and axial length after the injection. This contradiction of the AltanGoktas study may be due to small sample size or differences in axial length measurement in his study.

A recent study by H.S. Trehan reported that intravitreal injection of bevacizumab does not lead to changes in the intraocular pressure or anterior chamber depth that can lead to ocular damage in the short term.

Hoang in his study reported that transient or sustained IOP elevation cannot be predicted while taking into account axial length. Repeated trabecular meshwork trauma related to the absence or presence of reflux and immediate post-injection IOP elevation may be a contributing factor.

According to the biomechanical model developed by Kotliar and his colleagues, IOP elevation after intravitreal injection can be predicted or explained based on ocular biometric characteristics of the treated eye. Keeping in mind the biomechanical model developed by Kotliar, short axial length and a small intraocular volume in hyperopic eyes are more susceptible to extreme IOP elevation after intravitreal injection because of scleral rigidity, and a greater percentage of intraocular volume is introduced than in myopic eyes with long axial length.

It is a difficult task to quantify the reflux volume after intravitreal injection. Amount of reflux occurring after intravitreal Bevacizumab is accounted by various factors such as baseline intraocular pressure, the rigidity of sclera, the degree of liquefaction of the vitreous and the presence of a posterior vitreous detachment. Considering the ocular anatomic characteristics, such as high myopia linked with vitreous liquefaction, scleral thickness variations and biomechanics, and the presence of a posterior vitreous detachment, may result in lower IOP increases expected after IVB.

Conclusion:

The results of this study showed a remarkable transient increase in IOP after intravitreal injectionof bevacizumab. A significant inverse correlation was observed between axial length and IOP after intravitreal injections showing a meaningful association between these two variables.

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Authors' Affiliation

[1] **Dr Muhammad Mohsin Javaid**
VR Fellow (King Edward Medical University)
Email: lmdc99@hotmail.com

[2]**Professor Dr. Asad Aslam Khan**
MS, PhD
Professor and Head,
Institute of Ophthalmology,
Mayo Hospital, Lahore.
drasad@lhr.comsats.net.pk

[3]**Dr. Haroon Tayyab**
MBBS, FCPS (Ophth), FCPS(VRO), FICO
Asstt. Prof Vitreoretina
College of Ophthalmology &
Allied Vision Sciences (COAVS), Lahore.
Haroontayyab79@gmail.com

[4]**Dr. Ch Nasir Ahmed**
MBBS, FCPS. FVR, FICO
Asstt. Professor
Institute of Ophthalmology, &
Allied Vision Sciences (COAVS), Lahore.
Drnasirch1@gmail.com