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Intra-Vitreal Anti-Vegfs - Longterm Effect On Intraocular Pressure

[1]Ourfa Ashraf Wani, [2]Sheikh Sajjad, [3]Waseem Akram Khan
[1,3]Senior Resident, [2]Professor and HOD,
[1,2]Department of Ophthalmology, SKIMS-MCH, Srinagar, J&K
[3]Department of Medicine, SKIMS, Srinagar, J&K

***Corresponding Author:**
Dr. Ourfa Ashraf Wani
Senior Resident, Department of Ophthalmology, SKIMS-MCH, Srinagar, J&K

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Abstract

Aims and Objectives: The study was conducted to determine the long term effect of commonly used anti-VEGFs on intraocular pressure.

Materials and Methods: This was a Hospital based prospective, non-comparative, interventional clinical study conducted on 30 eyes that required treatment with intravitreal anti-VEGF drugs for various diseases like macular edema, due to diabetes , BRVO, CRVO, exudative age related macular degeneration etc. IOP was measured at baseline. Follow-up measurements of IOP were done at week 1,4,8,12,24 and 36. In patients that required multiple doses of the drugs, repeated intravitreal injections were given at 3 month interval.

Results:

The baseline mean IOP was 16.48 ±2.05 mmHg. Individual IOP was increased in 3 eyes (10%) 2 out of these 3 patients required continuous use of anti-glaucoma medication for the control of IOP for a brief interval, which then returned to the baseline at subsequent follow-ups. The mean IOPs at weeks 1, 4, 8, 12, 24 and 36 weeks were 17.24±1.96, 16.69±1.54, 16.90±1.37, 17.24±1.35, 16.76±1.35 and 16.97±1.15 respectively. P values being 0.155, 0.665, 0.370, 0.102, 0.548 and 0.274 at week 1, 4, 8, 12, 24 and 36 respectively when compared to baseline which were statistically insignificant.

Conclusion:

From this study it was concluded that intravitreal anti-VEGFs have no effect on intraocular pressure in the long run. After receiving intravitreal injections of anti-VEGF agents, a small proportion of non-glaucomatous eyes developed raised IOP which was controlled by antiglaucoma drugs but then returned to normal and no continuous IOP lowering agents were required.

Keywords: Anti-VEGFs, IOP, BRVO, CRVO, ARMD

Introduction

Anti-vascular endothelial growth factor (Anti-VEGF) therapy has revolutionised the treatment of retinal disease. Intravitreal anti-VEGFs are the mainstay for the treatment of choroidal neovascularization secondary to the neovascular age-related macular degeneration (ARMD), macular edema secondary to the retinal vein occlusion (RVO) and diabetic retinopathy (DR).[1,2,3,4] Commonly used intravitreal VEGF-antagonists are ranibizumab (Lucentis; Genentech/Novartis, Inc., San Francisco, CA, USA) and bevacizumab (Avastin; Genentech/Hoffmann-La Roche Inc., CA, USA). Intraocular pressure (IOP) elevation after an anti-VEGF injection can be acute and transient because of an increase in the ocular volume or a sustained rise in IOP, which may be related to the pharmacologic drug properties.[5,6,7,8] Anti-VEGF agents may directly damage the trabecular meshwork[9]. However, a study of cultured human cells treated with bevacizumab did not

demonstrate any toxic effects on trabecular meshwork cells[10]. Another possible mechanism is inflammation, such as drug-induced trabeculitis or uveitis[11]

Some authors believe that prophylactic use of 1% apraclonidine or timolol combined with brimonidine or dorzolamide may reduce both the magnitude and the duration of pressure peaks[12]. We conducted this study to see whether these intravitreal anti-VEGFs have any long term effect on the IOP elevations.

Aim Of The Study

To see the long term effects of intravitreal anti-VEGFs on intraocular pressure (IOP).

Materials And Methods

Our study was a Hospital based prospective, non-comparative, interventional clinical study conducted in the Department of Ophthalmology, SKIMS Medical College Hospital, Srinagar from 2019 to 2021. 30 eyes of 30 patients were taken in the study that required treatment with intravitreal anti-VEGFs for various diseases like macular edema, due to diabetes , BRVO, CRVO, exudative age related macular degeneration etc.

Inclusion Criteria

Patients of 18–85 years of age with initial IOP < 21 mmHg and ability to follow the scheduled visit protocol.

Exclusion Criteria

Patients with open-angle or angle-closure glaucoma, suspected glaucoma (IOP > 21 mmHg and/or cup to disc ratio > 0.5), currently receiving any anti-glaucoma medication, previously received any intravitreal injection of any medication (steroid or anti-VEGF agent), current use of steroid eye drops, and any ocular surface disease precluding a reliable IOP measurement.

Methods

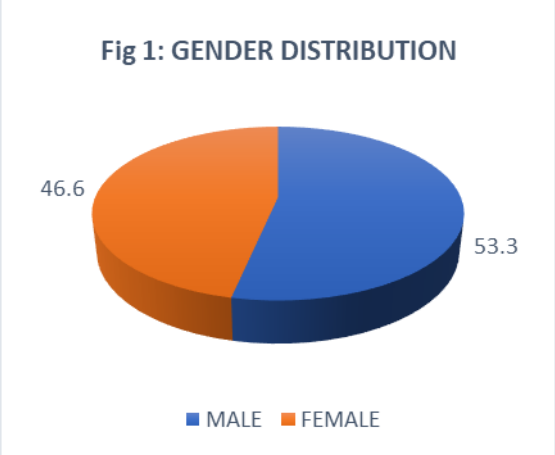
All the patients went through a standard examination protocol including:

Best corrected visual acuity testing, Slit lamp biomicroscopic examination of the anterior pole before mydriasis to identify cataract, iris neovascularization, posterior pole examination for diagnosis and Intraocular pressure measurement.

IOP was measured at baseline. Follow-up measurements of IOP were done at week 1,4,8,12,24 and 36. In patients that required multiple doses of the drugs, repeated intravitreal injections were given at 3 month interval. Timing of IOP measurement was scheduled according to the first injection. In case of the eye receiving the 3-monthly injection protocol, the second injection was usually given at the study visit and IOP measurement was obtained before the second injection of the protocol, to avoid the confounding effect from the short-term IOP rising. The same investigator obtained all IOP measurements. The mean IOP at each visit was obtained from the average of three measurements. Outcome measures included the means of IOP differences from baseline at each follow-up visit.

Results

Out of total 30 cases 16 (53.3%) were male and 14 (46.6%) were females Fig 1.



Out of 30 eyes, 33.33% were treated for diabetic macular edema, 8% for macular edema due to CRVO, 6% for maculae edema due to BRVO and 6% for wet ARMD, as shown in table 1.

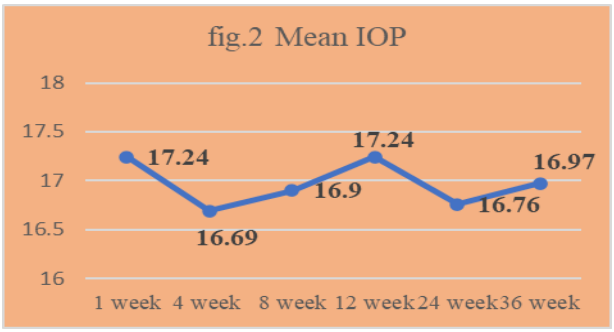
Table 1.

Disease profile	No. of patients	
Diabetic macular edema	10	33.33%
BRVO	6	20%
CRVO	8	26.66%
Wet ARMD	6	20%
Total	n=30	100%

The baseline mean IOP was 16.48 ±2.05 mmHg. Individual IOP was increased in 3 eyes (10%) 2 out of these 3 patients required continuous use of anti-glaucoma medication for the control of IOP for a brief interval, which then returned to the baseline at subsequent follow-ups. The mean IOPs at weeks 1, 4, 8, 12, 24 and 36 weeks were 17.24±1.96, 16.69±1.54, 16.90±1.37, 17.24±1.35, 16.76±1.35 and 16.97±1.15 respectively. P values being 0.155, 0.665, 0.370, 0.102, 0.548 and 0.274 at week 1, 4, 8, 12, 24 and 36 respectively when compared to baseline which were statistically insignificant, shown in table 2, fig.2

Table 2.

	IOP (mmHg) Mean ±SD	***T-stat***	***p-value***
Baseline	**16.48 ±2.05**	**--**	**--**
1 week	**17.24±1.96**	**-1.44**	**0.155**
4 week	**16.69±1.54**	**-0.44**	**0.665**
8 week	**16.90±1.37**	**-0.90**	**0.370**
12 week	**17.24±1.35**	**-1.67**	**0.102**
24 week	**16.76±1.35**	**-0.61**	**0.548**
36 week	**16.97±1.15**	**-1.11**	**0.274**



Discussion

Anti-VEGF drugs have changed the picture of various various diseases in ophthalmology in the recent past and is the main stay of treatment for various diseases. As we know that no treatment comes without any risks so this study was conducted to see whether these wonder drugs have any effect on the IOP in these patients. 30 eyes of 30 patients that met the inclusion criteria were taken in the study that required treatment with intravitreal anti-VEGFs for various diseases like macular edema due to diabetes , BRVO, CRVO, exudative age related macular degeneration etc. Out of total 30 cases 16 (53.3%) were male and 14 (46.6%) were females and were treated for diabetic macular edema in 33.33% patients, 8% for macular edema due to CRVO, 6% for maculae edema due to BRVO and 6% for wet ARMD.

The baseline mean IOP was 16.48 ±2.05 mmHg. After treatment with intravitreal anti-VEGFs the mean IOPs at weeks 1, 4, 8, 12, 24 and 36 weeks were 17.24±1.96, 16.69±1.54, 16.90±1.37, 17.24±1.35, 16.76±1.35 and 16.97±1.15 respectively. P values being 0.155, 0.665, 0.370, 0.102, 0.548 and 0.274 at week 1, 4, 8, 12, 24 and 36 respectively when compared to baseline which were statistically insignificant. Individual IOP was increased in 3 eyes (10%) 2 out of these 3 patients required continuous use of anti-glaucoma medication for the control of IOP, which then returned to the baseline at subsequent follow-ups. A similar study was conducted by Yoon Jeon Kim et al13 where 629 eyes with neovascular AMD and 95 eyes with RVO were taken in the study. Twenty eyes with neovascular AMD (3.0%) and 7 eyes with RVO (7.4%) experienced IOP elevation after multiple anti-VEGF injections, with an overall incidence of 3.7%. In the Cox proportional hazard analysis of total participants, a diagnosis of RVO (3.424, P = 0.005), a history of glaucoma (8.441, P = 0.001), and low baseline IOP (0.865, P = 0.040) were all significant risk factors for IOP elevation after multiple anti-VEGF injections. Thus suggesting a history of multiple intravitreal anti-VEGF injections was not a significant risk factor for IOP elevation in our study. IOP elevation was more common in eyes with RVO than with AMD after anti-VEGF injection. The results of this study were consistent with our study.

Good et al14 presented a study that included 215 eyes that were treated with Lucentis, Avastin, or both. IOP elevation was defined as an IOP of 22 mm Hg or greater with an elevation of 6 mm Hg or more, compared to pressure before the initiation of treatment, recorded in two consecutive measurements and lasting 30 days or more. Such persistent elevation was found in 6% of all eyes and required either topical treatment or laser trabeculoplasty. The average IOP in those eyes was 29 mm Hg (range, 23-36 mm Hg). The incidence of sustained IOP elevation was considerably greater in eyes with balanced pre-existing glaucoma (33%), compared to eyes without glaucoma (3.1%).

At the 2017 ARVO meeting in May, Dr. MacCumber and colleagues presented study findings indicating that overall anti-VEGF ther-apy was in fact associated with a small decrease in IOP over time.[15]

Conclusion:

Our study revealed that intravitreal anti-VEGFs have no long term effect on intraocular pressure. After receiving intravitreal injections of anti-VEGF agents, a small proportion (3%) of non-glaucomatous eyes developed raised IOP which was controlled by antiglaucoma drugs but then returned to normal and no continuous IOP lowering agents were required.

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