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INTRAOCULAR PRESSURE;

CHANGES IN INTRAOCULAR PRESSURE AFTER INTRA-VITREAL BEVACIZUMAB (ANTI VASCULAR ENDOTHELIAL GROWTH FACTOR) INJECTION IN NON-GLAUCOMATOUS PATIENTS.

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ABSTRACT… Objectives: To determine mean changes in intraocular pressure after intra-vitreal bevacizumab (anti vascular endothelial growth factor) in non-glaucomatous patients suffering from retinal vascular disorders. **Study Design:** Quasi experimental study. **Setting:** Outdoor patient Department of Layton Rahmatullah Benevolent Trust Free Eye Hospital, Lahore. **Period:** 06 months from Jan-2017 to June-2017. **Patients and Methods:** A total number of 100 patients having age 18-65 years who presented with retinal vascular disorders. Pre injection intraocular pressure was measured with Goldman Applanation Tonometer five minutes before injection. After that intravitreal bevacizumab was injected using standardized technique. Post-injection, intraocular pressure was measured after 1 month of injection. Data was analyzed with the help of SPSS v19. Paired sample t-test was applied to determine any significant difference in pre-injection and post-injection IOP at p-value of <0.05. Mean change in IOP was also calculated. **Results:** Mean age of patients was 51.76+9.22 Years. There were 50% male patients and 50% female patients. Diabetic retinopathy was diagnosed in 41% patients, central serous chorio-retinopathy in 17%, age related macular degeneration in 16%, branch retinal venous occlusion in 15% and idiopathic choroidal neovascularization in 11% patients. Right sided eye was affected in 53% patients. Mean pre-injection IOP was 14.07+3.15 and mean post-injection IOP was 14.54+2.31 mmHg (p-value 0.12). Mean difference in pre-injection and post-injection IOP (after 1 month of injection) was -0.523+2.98 mmHg. **Conclusion:** Bevacizumab can be safely administered for the treatment of non-glaucomatous retinal vascular disorders without significantly disturbing the IOP for a longer period of time.

Key words: Bevacizumab, Intra-ocular Pressure, Retinal Vascular Disorders.

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INTRODUCTION

Intravitreal anti vascular endothelial growth factors (VEGF) are commonly used for the treatment of chorioretinal neovascularization including retinal vein occlusion, diabetic retinopathy, age related macular disease and number of other ocular diseases.[1,2] In spite of potential but low rate of complications (e.g. endophthalmitis, retinal detachment, uveitis, cataract, retinal tear etc), the anti-vascular endothelial growth factors have become the treatment of choice and have gained worldwide acceptance and usage.[3] The known anti vascular endothelial growth factors are bevacizumab, ranibizumab, aflibercept and pegaptanib. Bevacizumab has comparable efficacy to ranibizumab, and low cost so it is commonly used in developing countries.[2] Bevacizumab is a humanized monoclonal IgG1 antibody recombinant that binds to vascular endothelial growth factor and prevents its binding to vascular endothelial growth factor receptor on endothelial cells. Reduction in activity of vascular endothelial growth factor inhibits angiogenesis and permeability.[4]

The introduction of fluid into the vitreal cavity has been established to raise intraocular pressure (IOP) immediately.[5] Increase in IOP is the most frequent reported complication of intravitreal injection, this increased IOP have negative effects on the blood supply of optic & retinal nerves and can damage the nerves. The reduction in blood supply is directly proportional to the increase in IOP.[6,7] A persistent increase in IOP requires the

use of anti-glaucoma medications to reduce IOP.[8-10] Very little is known about how long increased IOP persist after injection and does it need any intraocular pressure lowering therapy is not well determined. So in this study, we reassessed the changes in mean intraocular pressure induced by anti-vascular endothelial growth factor in non-glaucomatous patients suffering from retinal vascular disorders. This study will help us to establish local data. Another benefit of the study is that it can guide clinicians regarding the need of follow up of the patients to detect changes in IOP earlier and prevent complications if any, like optic nerve damage and visual field defects and the use of IOP lowering therapy.

PATIENTS AND METHODS

In this quasi experimental study, we included 100 patients of retinal vascular disorders. Study was conducted in Layton Rahmatullah Benevolent Trust (LRBT) Free Eye Hospital, Lahore within a duration of 06 months from Jan-2017 to June-2017. Patients with diagnosis of congestion, tortuosity, cotton spots, AV nipping (crossing of artery and vein), or any one of these on funduscopic were labelled as having retinal vascular disorders. Patients with baseline IOP ≤ 21 mmHg of any gender were included in this analysis. Patients with glaucoma, visual field defects, ocular surface disease causing inconvenience and non-reliability in measuring intraocular pressure and with Cup/disc ratio (C/D ratio) of optic nerve head ≥0.7 OR C/D ratio <0.7 with abnormal neuroretinal rim of the optic disc were excluded.

Intravitreal injection of 1.25 mg/0.05 ml of Bevacizumab using a 30 gauge needle was given using standard procedure in operative room under strict aseptic environment. Sterile cotton swab was placed over to eye to prevent reflux of fluid after injection. Post injection topical antibiotics (Moxifloxacin drops) were given to use 4 times in a day for one week after surgery.

IOP was measured five minutes before injection and after 1 month of intravitreal bevacizumab injection using Goldman Applanation Tonometer. IOP more than 21 mmHg after one month of injection was labelled as persistent increase in IOP.

All study related variables were entered in SPSS v19 windows software. Paired sample t-test was applied to determine any significant difference in pre-injection and post-injection IOP at p-value of <0.05. Mean change in IOP was also calculated.

RESULTS

The mean age of patients included in this study was 51.76+9.22 Years. In our study, there was equal proportion of male and female patients. There were 50% male patients and 50% female patients. There were 41% patients having diabetic retinopathy, 17% central serous chorio-retinopathy (CSCR), 16% presented with age related macular degeneration and 15% presented with branch retinal venous occlusion. There were only 11% patients who presented with idiopathic choroidal neovascularization. Most commonly affected eye was right eye, 53% patients presented with right sided eye disease, 46% with left sided eye disease and only one patient presented with both eyes problem (Table-I).

Pre-injection IOP of study patients was 14.07+3.15 mmHg and mean IOP pressure after 1 month of Bevacizumab injection was 14.54+2.31 mmHg. This difference in pre-injection and post-injection IOP was not significant statistically (p-value 0.12). Regarding mean change in IOP, post-injection IOP after one month was only 0.523+2.98 mmHg high as compared to the baseline IOP (Table-II). There was no incidence of persistent increase in IOP, and in all patients IOP was less than 21 mmHg after one month of injection.

Name of Variable	Value
Age	51.76+9.22
Gender (%)	
Male	50
Female	50
Diagnosis (%)	
DR	41
CSCR	17
AMD	16
BRVO	15
Idiopathic CNV	11
Affected Eye (%)	
Right	53
Left	46
Both Sides	1

Table-I. Data of baseline variables.

DR; diabetic retinopathy, **AMD;** Age related Macular Degeneration, **CSCR;** Central Serous chorio-retinopathy, **CNV;** choroidal neovascularization, **BRVO;** Branch Retinal Venous Occlusion.

	Intra-ocular Pressure		P-value
	Pre-injection	After One Month of Injection	
Mean	14.07	14.54	0.12
Standard Deviation	3.15	2.31	

Table-II. Comparison of pre-injection and Post-injection (after 1 month) IOP pressures.

DISCUSSION

Anti-VEGF have now become the standard treatment options for many ratino-vitreal diseases. The only concern of anti-VEGF administration is IOP spike because of increased volume inside the eye. Many studies have examined the rise in IOP after injection of anti-VEGF and concluded that the rise of IOP is transient and it returns to normal values with the passage of time and there is no need of additional interventions to reduce IOP after intra-vitreal injection of bevacizumab.[11-13] IOP may also increase as a result of inflammation, because bevacizumab is an antibody and contains some crystalloid fragments (Fc) that may bind with the immune particles e.g. complement system particles and may initiate inflammatory cascade.[14] Another mechanism is passing of high-molecular weight proteins into the anterior chamber through disrupted anterior hyaloid or disrupted zonules. The accumulation of anti-VEGF agents in the trabecula might also play a role.[15,16]

In present study, we investigated the effects of intra-vitreally injected bevacizumab on intra-ocular pressure within one month after injection in non-glaucoma patients having retinal vascular disorders. Mean age of our study patients was 51.76+9.22 Years. Mean age of patients in the study of Omay et al. was 63.58 ± 11.04 years.[17] Mean age of patients in the study of Lee et al. was 59.7 ± 13.6 years.[11] Mean age in our study was less as compared to their study.

In our study, there were 50% male patients and 50% female patients. There were 44.4% male patients and 55.6% female patients in the study of Kiddee et al.[18] Male and female ratio in our study was almost comparable to that study.

We did not found any significant difference in pre-injection and post-injection (after one month of injection) IOP. Mean pre-injection IOP was 14.07+3.15 mmHg and post-injection IOP was 14.54+2.31 mmHg and mean difference in pre-injection and post0injection IOP was -0.523+2.98 mmHg. Mean difference in IOP after 1 month of injection in the study of Kiddee et al. was -0.37+2.8 mmHg.[18] Mean difference in IOP in the study of Omay et al. was -1.59+4.18 mmHg. While pre-injection IOP was 16.77±4.47 mmHg and post-injection IOP was 15.19±4.68 mmHg.[17] This difference was not statistically significant as like to our study. Mean pre-injection intra-ocular pressure (IOP) in the study of Soheilian et al. was 14±2.2 mmHg and mean post-injection IOP after 3 months of injection was 13.4±2.1 mmHg. This difference in mean pre-injection and post-injection IOP after 3 months of injection was not statistically significant.[19] The major difference in this study and present study was, we measured IOP after 1 month of injection and they measured IOP after 3 months of injection.

CONCLUSION

In this study, there was no significant change in mean intraocular pressure (after 1 month of injection) after intra-vitreal bevacizumab (anti vascular endothelial growth factor) in non-glaucomatous patients suffering from retinal vascular disorders. So bevacizumab can be safely administered for the treatment of non-glaucomatous retinal vascular disorders without significantly disturbing the IOP for a longer period of time.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Muhammad Tahir	Conceived designed and wrote the manuscript.	
2	Tariq Mehmood Qureshi	Supervised the research project and did final approval for publication of manuscript.	
3	Sehrish Abbas	Did data collection and compilation.	