DOI: https://doi.org/10.53350/pjmhs020231712422

ORIGINAL ARTICLE

The Impact of Intravitreal Avastin on Systemic Blood Pressure in Patients Under Blood Pressure Control

BILAL KHAN[1], JAVED UR RAHMAN[2], NESR FAROOQ[3], AYYAZ HUSSAIN AWAN[4], MUHAMMAD ZIA IQBAL[5], SAAD MUSHTAQ MALIK[6], NAZLI GUL[7]

[1]*Assistant Professor Ophthalmology department Khyber Medical College/ Khyber Teaching Hospital, Peshawar*
[2]*Chief Consultant & HOD, Department of Ophthalmology Shaheed Saif ur Rehman, Government Teaching Hospital, Gilgit.*
[3]*Assistant Professor, Department of Ophthalmology, Shalamar Medical and Dental College, Lahore*
[4]*Associate Professor, Department of Ophthalmology, Farooq Hospital/ Akhtar Saeed Medical College, Rawalpindi*
[5]*Ophthalmologist & Professor of Anatomy, Department of Basic Sciences, Sulaiman Alrajhi University Al Bukayriyah, Al Qaseem, KSA*
[6]*Classified Eye Specialist, Assistant Professor of Ophthalmology, Eye Department, CMH Multan, CIMS Medical College, Multan*
[7]*Assistant Professor, Department of Ophthalmology, Khyber Medical College/ Khyber Teaching Hospital, Peshawar*
Correspondence to: Nazli Gul, Email: drnazli83@gmail.com

ABSTRACT

Objective: The objective of this study was to examine how intravitreal avastin affected systemic blood pressure in patients with managed hypertension.

Methods: Seventy patients with retinal vascular diseases were included in this study. Blood pressure readings were taken from patients before intravenous administration (IVA) to establish a baseline, then again 1 day, 1 week, 4 weeks, and finally monthly for a minimum of 3 months. Avastin was administered intravitreally at a concentration of 0.05 ml to all patients. Data was examined with the help of SPSS 22.0.

Results: There were 38 (54.3%) males and 32 (45.7%) females among all cases. Patients mean age was 65.13±8.37 years. On the first day after injection, 92% of patients noticed an increase in blood pressure compared to their baseline. At the 1-week, 4-week, and other time points, there were no statistically significant changes in blood pressure. following injection.

Conclusion: Our study found that intravitreal avastin is safe for treating ocular vascular disorders in patients with controlled hypertension.

Keywords: systemic blood pressure, avastin, digital sphygmomanometer, ocular pathology.

INTRODUCTION

Since its discovery in 1989, the protein vascular endothelial growth factor (VEGF) has been recognized for its ability to increase capillary permeability and regulate the proliferation of endothelial cells. Adult and fetal blood vessel development are dependent on it. Because of its important function in controlling angiogenesis, VEFG[1] is an attractive pharmacologic alteration target for the treatment of cancer and eye diseases. Bevacizumab is a recombinant human monoclonal antibody that targets VEFG; it has been used as an antiangiogenic medication to treat tumors including renal cell carcinoma, colorectal carcinoma, and breast cancer.a subsequent Oedematous, proliferative, and intraocular neovascular disorders have recently seen an increase in the "off-label" intravitreal injection of anti-VEFG medicines such as bevacizumab.[2-4]

Hypertension is still largely unexplained, despite being one of the most common disorders. Heart failure, stroke, and myocardial infarction are hypertension-related complications that significantly raise healthcare expenditures. Having hypertension, and systolic hypertension in particular, is more common in older individuals. So, new ways of lowering blood pressure and finding people who are more likely to have issues could be very helpful to public health. According to studies conducted with bevacizumab, hypertension can be caused or made worse in certain people by blocking VEFG. Five, four Although not yet proved, the theory that nitric oxide (NO) mediates the hypertension that develops after antiangiogenic treatment is widely held. Preclinical in vivo studies have shown that vascular endothelial growth factor (VEGF) boosts arterial pressure by activating the protein kinase-C pathway.

This is why there is ongoing controversy regarding the systemic safety of intravitreal anti-VEFG medication, especially in individuals at high risk for cardiovascular disease. Data from meta-analyses for age-related macular degeneration suggests that cerebrovascular events are more likely to occur with monthly dose compared to as-needed medication.[6]

Intravitreal anti-VEFG injections are frequently used in diabetics with retinopathy and concurrent nephropathy; thus, it is crucial to carefully observe any changes in proteinuria and blood pressure after their delivery. After entering the bloodstream, anti-VEFG medications actively block VEFG activity in living creatures, according to recent studies[7]. Further research shows that after one week of intravitreal injection, anti-VEFG medications attach to and harm the glomerular basement membranes in monkey glomeruli[8]. After intravitreal injections of anti-VEFG medications, the "fellow eye effect" is the most desirable side effect compared to others. One study found that injecting an anti-VEFG medication into one eye reduced the severity of diabetic retinopathy in the other eye[9].

Patients with AMD, or age-related macular degeneration, were found to have systemic absorption, according to Avery et al.[10]. A subsequent study in patients with diabetic macular edema and central retinal vein occlusion confirmed these results[10]. Modern pharmacodynamic studies confirmed serum values of 0.1-0.2 nmol/L, in agreement with FDA-disclosed results. According to Avery et al.[11], these values were comparable to or greater than the 50% inhibitory concentrations (IC50) of a drug called be aflibercept, and ranibizumab, respectively. Ranibizumab has the lowest drug absorption following intravitreal injection and the lowest degree of systemic VEFG inhibition, according to both trials[10,11]. These findings were validated by Rogers et al. through analysis of the IVAN research participants. "Impairment of VEFG in Related to age Choroidal Neovascularization" is what it implies. Intravitreal bevacizumab and aflibercept were more effective in reducing systemic VEFG than intravitreal ranibizumab.

This study aimed to evaluate the variation in avastin concentration between systemic and intravitreal doses in order to assess the impact of intravitreal avastin on systemic blood pressure in hypertension patients whose hypertension was well-controlled.

MATERIALS AND METHODS

The study was conducted in Khyber Teaching Hospital, Peshawar during May 2022 to June 2023. In this retrospective study 70 patients were presented. They suffered from chronic macular edema, age-related macular degeneration, central retinal vein occlusion, proliferative diabetic retinopathy, and other ocular vascular disorders. A comprehensive ophthalmic evaluation was performed on all patients, which included biomicroscopic fundus examinations, slit-lamp evaluations, and Snellen visual acuity measures. The diagnosis was confirmed by fluorescein fundus

Received on 20-07-2023
Accepted on 05-11-2023

angiography, which may be performed with or without optical coherence tomography. The patients' hypertension was under control. Patients without hypertension, those with uncontrolled hypertension, and those with glaucoma are not eligible.

The blood pressure was taken in the supine position of each patient using the same technique, which involved letting them sit in a quiet room for almost half an hour before using a digital sphygmomanometer with the appropriate cuff. The blood pressure was taken immediately prior to the bevacizumab injection (baseline), and then again on days 1, weeks 1, and 4, and then monthly for three months.

We excluded patients from the analysis and sent them to an internist for further testing if their baseline systolic and diastolic blood pressure levels were 140 and 90 mm Hg, respectively. The sole operation performed on each patient in this research was injecting 0.05 ml of 1.25 mg bevacizumab intravitreally. Applying 5% povidone-iodine drops to the eye's surface after tetracaine numbs it was a two-minute process. The next step was to apply a 10% scrub of povidone-iodine to the eyelids and lashes, followed by the insertion of a sterile speculum between the eyelids. By inserting a 30-gauge needle into the vitreous cavity through the pars plana a structure situated 3.5 mm posterior to the limbus 0.05 ml (1.25 mg) of Bevacizumab (Avastin) was administered.

To rule out central retinal artery occlusion, light perception was tested following the procedure. After that, over the first seven days, everyone was directed to administer antibiotic eye drops on the injected eye four times a day. Each patient was told about the potential dangers connected with this operation.

RESULTS

There were 38 (54.3%) males and 32 (45.7%) females among all cases. Patients mean age was 65.13±8.37 years. Most common comorbidity was hypertension followed by diabetes and stroke. (Table 1)

As per ocular pathology 28 cases had diabetic retinopathy, 23 cases had choroidal neovascularization, retinal vein occlusion was found in 12 cases and macular edema in 7 cases.(figure 1)

Table-1: Demographics of the presented cases

Variables	Frequency/Percentage
Gender	
Male	38 (54.3%)
Female	32 (45.7%)
Mean age (years)	65.13±8.37
Comorbidities	
HTN	32 (45.7%)
DM	21 (30%)
Stroke	17 (24.3%)

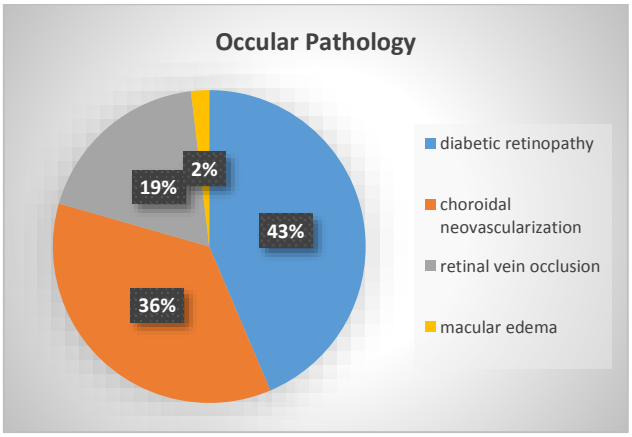

Figure-1: Distribution of the cases with respect to ocular pathology

On the first day after injection, 92% of patients noticed an increase in blood pressure compared to their baseline. At the 1-week, 4-week, and other time points, there were no statistically significant changes in blood pressure. following injection.(table 2)

Table-2: Variations in Blood Pressure

Variables	Systolic (Bp)	Diastolic (Bp)
Baseline	123±14	73±11
1 day	134±13	85±20
1 week	133±14	80±17
4 week	132±10	80±12
4months	130± 9	82±14

DISCUSSION

Ophthalmologists have been using bevacizumab and other drugs to treat neovascular eye problems in the past few years. Scientific evidence indicates that this treatment is successful. These conditions include choroidal neovascularizations (sometimes called age-related macular degeneration), neovascular glaucoma, diabetic retinopathy, retinal vascular occlusion, and retinopathy of prematurity. Intravitreal administration of bevacizumab does not cause major intraocular toxicity. There are situations in which this could happen. Our research shows that the first day after an injection, blood pressure shows a small improvement. This might not be a medical adverse effect at all, but rather the result of the emotional and mental strain of the operation itself. The reason behind this is because the highest concentration of avastin in the blood was observed anywhere from five to eight days after the injection[12].

Several studies investigated the effects of bevacizumab administered intravitreally and focused on this mode of administration. Bypassing the central nervous system was the goal of this delivery method for avastin. The potential local adverse effects of this surgical treatment were the subject of investigations at multiple institutions. Our study found only subconjunctival bleeding, but some of these patients also had endophthalmitis, visual hallucinations, tractional retinal detachment, uveitis, and changes in intraocular pressure (IOP)[13–17].

After the procedure, the researchers also tracked the patient's systemic blood pressure to see how it changed. The vast majority of these studies found no adverse effects on blood pressure from intravitreal bevacizumab injection. This held true irrespective of the presence or absence of ocular illness. The results of the study carried out by Chung and colleagues in the Republic of Korea[18] indicated that this was indeed the case. Our investigations and their studies yielded identical results when we compared the inquiry's findings. Additional Turkish research by Rasier and colleagues found that intravitreal bevacizumab injections put hypertensive patients at risk of blood pressure dysregulation or hypertension progression[19]. The results of the research corroborated this.

CONCLUSION

It has been observed that patients with controlled hypertension, irrespective of ocular disease, can safely receive intravitreal bevacizumab.

REFERENCES

1. Ferrara N, Hillan KJ, Gerber HP, Novotny W . Discovery and development of bevacizumab, an anti-VEGF antibody for treating cancer. *Nat Rev Drug Discov* 2004; **3**: 391–400.
2. Chen Y, Wiesmann C, Fuh G, Li B, Christinger HW, McKay P *et al*. Selection and analysis of an optimized anti-VEGF antibody: crystal structure of an affinity-matured Fab in complex with antigen. *J Mol Biol* 1999; **293**: 865–881.
3. Rosenfeld PJ, Heier JS, Hantsbarger G, Shams N . Tolerability and efficacy of multiple, escalating doses of ranibizumab (Lucentis) for neovascular age-related macular degeneration. *Ophthalmology* 2006; **113**: 623–632.
4. Singer RB, Milano AF . Mortality in co-morbidity (I) Analysis of the results in the Multiple Medical impairment Study for impairments with elevated blood pressure as the second or co-morbid impairment. *J Insur Med* 2007; **39** (2): 78–88.

5. Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB *et al*. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *JAMA* 2002; **287**: 1003–1010.
6. Wu L, Martínez-Castellanos MA, Quiroz-Mercado H, Arevalo JF, Berrocal MH, Farah ME *et al*. Twelve-month safety of intravitreal injections of bevacizumab (Avastin): results of the Pan-American Collaborative Retina Study Group (PACORES). *Graefes Arch Clin Exp Ophthalmol* 2008; **246**: 81–87.
7. Kernt M, Neubauer AS, Kampik A . Intravitreal bevacizumab (Avastin) treatment is safe in terms of intraocular and blood pressure. *Acta Ophthalmol Scand* 2007; **85**: 119–120.
8. Avery RL, Castellarin AA, Steinle NC et al. Systemic pharmacokinetics following intravitreal injections of ranibizumab, bevacizumab or aflibercept in patients with neovascular AMD. Br J Ophthalmol 2014; 98: 1636–1641
9. schulakow A, Christner S, Julien S et al. Effects of a single intravitreal injection of aflibercept and ranibizumab on glomeruli of monkeys. PLoS One 2014; 9: e113701
10. Avery RL, Castellarin AA, Steinle NC et al. Systemic pharmacokinetics and pharmacodynamics of intravitreal aflibercept, bevacizumab, and ranibizumab. Retina 2017; 37: 1847–1858
11. Rogers CA, Scott LJ, Reeves BC et al. Serum vascular endothelial growth factor levels in the IVAN trial; relationships with drug, dosing, and systemic serious adverse events. Ophthalmol Retina 2018; 2: 118–127
12. Ziemssen F, Zhu Q , Peters S, Grisanti S, El Wardani M, Szurman P et al. Intensified monitoring of circadian blood pressure and heart rate before and after intravitreous injection of bevacizumab: preliminary findings of a pilot study. Int Ophthalmol 2009; 29: 213–224
13. FALKENSTEIN, IRYNA A. CHENG et al. Changes of Intraocular Pressure After Intravitreal Injection of Bevacizumab (Avastin) October 2007 - Volume 27 - Issue 8 - pp 1044-1047
14. MASON, JOHN O, MILTON et al. Incidence of Acute Onset Endophthalmitis Following Intravitreal Bevacizumab (Avastin) Injection April 2008 - Volume 28 - Issue 4 - pp 564-567.
15. Arevalo JF, Maia M, Flynn HW et al. Tractional retinal detachment following intravitreal bevacizumab (Avastin) in patients with severe proliferative diabetic retinopathy. Br J Ophthalmol 2008; 92:213-216.
16. PIERAMICI, DANTE J, AVERY et al. Case of Anterior Uveitis After Intravitreal Injection of Bevacizumab. September 2006 - Volume 26 - Issue 7 - pp 841-842
17. Mitrut I, Chua P, Aslam T et al. Short-term changes of visual hallucinations after intravitreal injection of ranibizumab in neovascular age-related macular degeneration. Eye (2010) 24, 1825
18. Chung YR, Lee K, Cho EH et al. Blood pressure changes after intravitreal bevacizumab in patients grouped by ocular pathology. Eye (2010) 24, 1320–1324
19. Rasier R, Artunay O, Yuzbasioglu E et al. The effect of intravitreal bevacizumab (avastin) administration on systemic hypertension. Eye (2009) 23, 1714–1718.

This article may be cited as: Khan B, Rahman JU, Farooq N, Awan AH, Iqbal MZ, Malik SM, Gul N: The Impact of Intravitreal Avastin on Systemic Blood Pressure in Patients Under Blood Pressure Control. Pak J Med Health Sci, 2023; 17(12): 422-424.