ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EFFECT OF PROPHYLACTIC INTRAOCULAR PRESSURE LOWERING MEDICATION (BRINZOLAMIDE) ON INTRAOCULAR PRESSURE AFTER RANIBIZUMAB INTRAVITREAL INJECTION: A COMPARATIVE STUDY.

Ophthalmology

Dr KaliShankar Das Assistant professor ,Nil Ratan Sircar Medical college and Hospital, Kolkata

Dr Athokpam Poireiton* Post graduate trainee ,Nil Ratan Sircar Medical College and Hospital, Kolkata*Corresponding Author

ABSTRACT

Aim: To evaluate the effect of prophylactic intraocular pressure (IOP)-lowering medication (brinzolamide) on IOP after ranibizumab intravitreal injections (IVIs). Materials and Methods: This is prospective cohort study which included 400 eyes from 400 patients (1 eye per patient) who were treated with ranibizumab intravitreal injection. Two hundred and twenty-two (222) patients in control group had received the ranibizumab IVI, but 178 patients in case group received one drop of prophylactic intraocular brinzolamide pre injection. The IOP was measured by noncontact tonometer before injection, at 10, 30, 120 min and 1 day after injection in a sitting position. Results: The mean IOP measured before injection, at 10, 30, 120 min and 1 day after injection individually among cases and control groups. Comparing two groups, the mean increase on IOP was statistically significant at 10, 30, 120 min post injection ($P < 0.05$). Conclusions: IVI of ranibizumab causes a considerable short-term transient rise on IOP in most patients. The effect of prophylactic IOP-lowering medication on IOP after IVIs can be statistically significant from 10 min to 2 h after IVIs.

KEYWORDS

Brinzolamide, intraocular pressure, intravitreal injection ranibizumab.

INTRODUCTION-

Recently, the administration of intravitreal injection anti-vascular endothelial growth factor(anti-VEGF) agents has become a new application for treating a variety of retinal and choroidal neo-vascular diseases including neovascular age-related macular degeneration (AMD), central vein or branch vein occlusion with macular edema, and diabetic maculopathy.[1-3]Anti-VEGF drugs include the Food and Drug Administration-approved agent ranibizumab (Lucentis) which are VEGF-A inhibitors and the off-label use of bevacizumab (Avastin). Injection of ranibizumab into vitreous cavity obviously increases the intraocular volume by adding fluid, which can induce an increase in intraocular pressure (IOP) and can vary according to globe size, injected volume, scleral thickness, and scleral rigidity. [4,5]

As the number of IVIs is growing, it is important to make sure these treatments are safe for patients. Till date many reports have published that the injections may cause immediate or sustained IOP change. [6-11] Although these IOP elevation are common, it is unknown whether repeated IOP spikes may cause damage in predisposed eyes. Studies noted that even transient IOP elevations can be associated with visual field defects [12] although sustained ocular hypertension can lead to significant optic nerve damage is well-known. Therefore, it may be necessary to control the IOP after IVI. Although both transient and sustained pressure rise after ranibizumab IVI are studied extensively in the Western population, [13] the conclusions about the effectiveness of IOP-lowering medications in preventing IOP increase after IVI from some studies are different. Studies suggested that routine prophylactic use of IOP-lowering medications is essentially ineffective in preventing IOP spikes after IVI.[14] Thereby, we investigated this prospective cohort study aiming to observe the effect of prophylactic IOP-lowering medication on IOP after ranibizumab IVIs.

Materials and Methods –

This prospective study followed the principles of the Declaration of Helsinki and all participants signed a standard informed consent form reporting the potential risks and benefits of the procedure and subsequent management. All patients were confirmed by the Department of Ophthalmology, NRS Medical College and Hospital for a detailed examination including best-corrected visual acuity (BCVA) and IOP, slit-lamp bio microscopy, auto refractometry, gonioscopy, and dilated fundoscopic examinations of both eyes.

The study included 400 eyes from 400 patients (1 eye per patient) diagnosed exudative AMD, diabetic macular edema (DME), retinal vein occlusion (RVO), pathologic myopia (PM), idiopathic choroidal neovascularization (ICNV), or cystoid macular edema (CME) who were treated with ranibizumab (0.5 mg/0.05 ml) IVI between June 2018 and May 2020 over a period of two years. Exclusion criteria included younger than 18 old years, ocular hypertension before injection, family history or a prior diagnosis of glaucoma, prior vitrectomy or phacoemulsification surgery, use of IOP-lowering agents, allergy to sulfur/sulphonamide-containing drugs. All the patients were divided randomly into two groups. In control group, 222patients (mean ± standard deviation [SD], 64.21 ± 14.10 years) only received the ranibizumab IVI while in case group, 178 patients (mean ± SD, 61.54 ± 14.60 years) received one drop of prophylactic intraocular brinzolamide before ranibizumab IVI. The IOP was measured by noncontact Topcon tonometry (Japan) during the study. To start the operation, ranibizumab injection was given in upper pars plana with 30-gauge needle after processing a complete sterile draping and rinsed with topical povidone-iodine under a topical anesthesia of Proparacaine eye drops. The injection site was located 3.5 mm posterior to the limbus. Both before and after IVI, patients were treated with Moxifloxacin eye drops for 5 days. The IOP were measured before injection, at 10, at 30, at 120 min and at 1 day after injection in a sitting position. One drop of brinzolamide was used after the baseline IOP measurement approximately 2 h (mean ± SD, 112.05 ± 26.61 min) before injection.

Statistical analysis –

Statistical analysis was performed using SPSS (version 17.0) software (SPSS Inc., Chicago, IL, USA). Kolmogorov–Smirnov test of nonparametric analysis and Chi-square test were used to analyze the data of two groups. We set $P < 0.05$ (two-sided) with statistical significance in this study.

Results-

All patients completed each IOP measurement. The diagnoses of patients were done as follows: Exudative AMD, DME, RVO, PM, ICNV, and CME. None of the study patients has significant intraoperative or shorter-term postoperative complications of operation or drugs such as endophthalmitis, hypersensitive to brinzolamide, or ranibizumab except high IOP. The baseline characteristics shows that the differences were not significant in gender, age, study eye, BCVA, and number of IVIs ($P > 0.05$) between two groups.

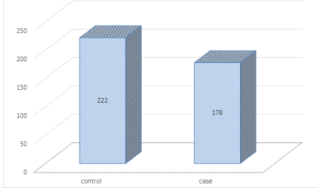

Fig 1. frequency of groups

Data taken included IOP measurements of baseline and immediately at 10, 30, 120 min and 1 day after IVIs. The mean IOP measured before injection, at 10, at 30, at 120 min and at 1 day after injection individually were 15.79 ± 2.21 mmHg, 19.33 ± 4.86 mmHg, 16.64 ± 2.93 mmHg, 16.17 ± 3.13 mmHg, and 15.07 ± 2.55 mmHg in case group and 15.82 ± 2.57mmHg, 21.34 ± 5.88mmHg, 18.17 ± 4.06mmHg, 17.59 ± 4.42 mmHg, and 15.48 ± 2.92 mmHg in control group. The tendency in both curves is a sharp increase on IOP a few minutes after injection, with a gradual decline over the next hours. Maximum IOP elevation occurred at the time point of 10 min after injection in both groups. At time points of 10, 30, and 120 min post-injection, mean IOP was significantly higher in control group when compared with the case group ($P < 0.05$); however, the differences were not significant at baseline and after 1 day ($P = 0.463$). The mean post-injection IOP for control group at the time points of 10, 30, and 120 min was statistically different when compared with baseline IOP ($P < 0.05$). On the contrary, in case group, this difference was observed only for the time point of 10 min ($P < 0.05$).

Comparing two groups by Chi-square test, it indicated that the ratio of IOP ≥21 mmHg and the elevation of IOP ≥5 mmHg within 2 h after injection had significant difference as Tables 1 showed ($P < 0.05$)

Table1: Comparison of elevation in IOP >= 5mmHg

Time	Case (178)	Control (222)	p-value	OR	95%CI
10 min after	64	120	0.001	0.482	0.311-0.742
30 min after	8	42	0.000	0.183	0.074-0.444
120min after	6	38	0.000	0.200	0.083-0.494
24 hrs. after	0	2	0.642	0.451	0.046-4.375

DISCUSSION

We found that in case group of our study, patients use prophylactic IOP-lowering medication (brinzolamide) before injection have statistically significance only at 10 min after IVI. When comparing with the control group, the significant difference was observed up to 2 h. No matter the ratio of IOP ≥21 mmHg or elevation of IOP ≥25 mmHg, the results are similar within 2 h. Frenkel et al. reported that the IOP reduced to < 30 mmHg in all patients within 20 min.14 But, study suggested that 13% of eyes with 30 mmHg or greater 30 min after injection. However, they all indicated that prophylactic medication may not be necessary to prevent post injection IOP spikes.[15,16]

We also found that the IOP increase after IVI in the control group of our study persisted for short period. Until 2 h after IVI, the IOP increase was statistically significant but no significance after 1 day. Similarly, a study reported that transient IOP increases within 30 min after IVI, however, there were no significant differences after half an hour.7 Other studies on IVI have reported transient IOP increases after 30–60 min, and stabilizing at baseline values after 1 day.[4,8] The little differences could be related to differences in the population race studied and/or IOP measurement techniques.

The volume of the vitreous cavity in human eye is 4 ml approximately, and the volume of ranibizumab injected into the vitreous is 0.05 ml. Therefore, the increase in fluid volume of the vitreous cavity is 1.25% approximately, which may cause immediate IOP elevation. The block hypothesis for the potential mechanisms inducing an IOP elevation after IVI is that medications may block the immediate aqueous humor cycle channels, including the trabecular meshwork or Schlemm's canal outflow pathways by an unclear mechanism for several weeks or months.[10] Although these hypotheses are related to the sustained increased IOP, they may indicated that the ocular structure of patients with IVI have changed and are sensitive to the changes of the volume of the vitreous cavity. In addition, the daily fluctuation of the IOP may also play a role in the elevation of the IOP.

Studies reported that the prophylactic administration of antiglaucoma tic drugs before intravitreal anti-VEGF injection effectively reduced the early IOP elevation.16Similarly, in our study, under prophylactically using brinzolamide, the significant difference of IOP after injection between two groups is obvious within 2 h which may indicate that brinzolamide can successfully suspend the IOP rise.

CONCLUSIONS

IVI of ranibizumab causes a considerable short-term transient rise on IOP in most patients. The effect of prophylactic IOP-lowering medication (brinzolamide) on IOP after IVIs can be statistically significant from 10 min to 2 h after IVIs. This study helps to illustrate the effect of prophylactic IOP-lowering medication on IOP after ranibizumab IVIs and whether the IOP-lowering therapy is necessary after IVIs. Therefore, further larger multiple centers studies are needed to make a definite conclusion.

REFERENCES

1. Bandello F, De Benedetto U, Knutsson KA, Parodi MB, Cascavilla ML, Iacono P. Ranibizumab in the treatment of patients with visual impairment due to diabetic macular edema. Clin Ophthalmol 2011; 5:1303-8.
2. Arias L, Planas N, Prades S, Caminal JM, Rubio M, Pujol O, et al. Intravitreal bevacizumab (Avastin) for choroidal neovascularization secondary to pathological myopia: 6-month results. Br J Ophthalmol 2008; 92:1035-9.
3. Costa RA, Jorge R, Calucci D, Melo LA Jr., Cardillo JA, Scott IU. Intravitreal bevacizumab (avastin) for central and hemicentral retinal vein occlusions: IBeVO study. Retina 2007; 27:141-9.
4. Pallikaris IG, Kymionis GD, Ginis HS, Kounis GA, Tsilimbaris MK. Ocular rigidity in living human eyes. Invest Ophthalmol Vis Sci 2005; 46:409-14.
5. Kotliar K, Maier M, Bauer S, Feucht N, Lohmann C, LanzlI. Effect of intravitreal injections and volume changes on intraocular pressure: Clinical results and biomechanical model. Acta Ophthalmol Scand 2007; 85:777-81.
6. Gismondi M, Salati C, Salvetat ML, Zeppieri M, Brusini P. Short-term effect of intravitreal injection of ranibizumab (Lucentis) on intraocular pressure. J Glaucoma 2009; 18:658-61.
7. Mojica G, Hariprasad SM, Jager RD, Mieler WF. Short-term intraocular pressure trends following intravitreal injections of ranibizumab (Lucentis) for the treatment of wet age-related macular degeneration. Br J Ophthalmol 2008; 92:584.
8. Choi DY, Ortube MC, McCannel CA, Sarraf D, Hubschman JP, McCannel TA, et al. Sustained elevated intraocular pressures after intravitreal injection of bevacizumab, ranibizumab, and pegaptanib. Retina 2011; 31:1028-35.
9. Tseng JJ, Vance SK, Della Torre KE, Mendonca LS, Cooney MJ, Klancnik JM, et al. Sustained increased intraocular pressure related to intravitreal antivascular endothelial growth factor therapy for neovascular age-related macular degeneration. J Glaucoma 2012; 21:241-7.
10. Dedania VS, Bakri SJ. Sustained elevation of intraocular pressure after intravitreal anti-vegf agents: What Is the Evidence? Retina 2015; 35:841-58.
11. SooHoo JR, Seibold LK, Kahook MY. The link between intravitreal antivascular endothelial growth factor injections and glaucoma. Curr Opin Ophthalmol 2014; 25:127-33.
12. Tsamparlakis JC. Effects of transient induced elevation of the intra-ocular pressure on the visual field. Br J Ophthalmol 1964; 48:237-49.
13. Frenkel MP, Haji SA, Frenkel RE. Effect of prophylactic intraocular pressure-lowering medication on intraocular pressure spikes after intravitreal injections. Arch Ophthalmol 2010; 128:1523-7.
14. HeierJS, AntoszykAN, Pavan PR, Leff SR, Rosenfeld PJ, Ciulla TA, et al. Ranibizumab for treatment of neovascular age-related macular degeneration: A phase I/II multicenter, controlled, multidose study. Ophthalmology 2006; 113:633. e1-4.
15. Hariprasad SM, Shah GK, Blinder KJ. Short term intraocular pressure trends following intravitreal pegaptanib (Macugen) injection. Am J Ophthalmol 2006; 141:200 1.
16. Kim GN, Han YS, Chung IY, Seo SW, Park JM, Yoo JM. Effect of Dorzolamide/Timolol or Brinzolamide/Timolol prophylaxis on intravitreal anti-VEGF injection-induced intraocular hypertension. Semin Ophthalmol 2013; 28:61-7.