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Immediate Intraocular Pressure Dynamics Following Intravitreal Aflibercept, Ranibizumab and Faricimab: A Prospective Comparative Study

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Abstract: ***Background / Aims: Intravitreal administration of anti–vascular endothelial growth factor agents is the cornerstone of treatment for common retinal vascular disorders. A transient rise in intraocular pressure (IOP) following injection is a recognised immediate effect, but the magnitude and pattern of this rise may vary among different agents. This study aimed to compare short-term post-injection IOP changes following intravitreal aflibercept, ranibizumab and faricimab. Methods: This prospective, observational study included 75 patients diagnosed with neovascular age-related macular degeneration or diabetic macular oedema. Patients were equally allocated into three groups receiving intravitreal aflibercept 2 mg, ranibizumab 0.5 mg or faricimab 6 mg. IOP was measured using a iCare IC200-tonometer prior to injection (T0) and at 30 seconds (T1), 5 minutes (T2) and 15 minutes (T3) following injection. Changes in IOP over time within each group and differences between treatment groups were analysed. Any occurrence of acute visual loss necessitating intervention was recorded. Results: A significant elevation in IOP was observed in all treatment groups at 30 seconds post-injection (T1). The mean IOP rise at T1 was highest in the aflibercept group (43.40 ± 9.80 mm Hg), followed by ranibizumab (42.20 ± 10.10 mm Hg), while faricimab demonstrated a comparatively lower initial increase (34.10 ± 8.60 mm Hg). By 5 minutes post-injection, IOP values declined substantially, with no statistically significant differences between the groups. At 15 minutes, mean IOP had returned to near-baseline levels in all eyes. No patient developed sustained visual impairment or required anterior chamber paracentesis. Conclusion: Intravitreal aflibercept, ranibizumab and faricimab are associated with a brief but marked rise in IOP immediately following injection, which resolves rapidly within 15 minutes. Faricimab produces a lower early IOP spike compared with aflibercept and ranibizumab; however, overall short-term IOP behaviour is comparable among the three agents.***

Keywords: Intraocular pressure, Intravitreal injections, Anti-vascular endothelial growth factor, Aflibercept, Ranibizumab, Faricimab, Age-related macular degeneration, Diabetic macular oedema

1.Introduction

Intravitreal inhibition of vascular endothelial growth factor (VEGF) has become the cornerstone of management for retinal vascular diseases since its introduction in clinical practice in 2004. Anti-VEGF therapy is now the first-line treatment for conditions such as neovascular age-related macular degeneration (nAMD)[1], diabetic macular oedema (DMO)[2] and macular oedema secondary to retinal vein occlusion[3], resulting in significant improvements in visual outcomes and altering treatment goals from vision preservation to visual restoration.[4]

Although intravitreal anti-VEGF agents are highly effective, their use is associated with several ocular adverse effects.[5 6 7] Among these, a transient elevation in intraocular pressure (IOP) immediately following injection is a well-recognised early phenomenon. This acute IOP rise is thought to result primarily from a sudden increase in intraocular volume and is influenced by factors such as injection volume, ocular rigidity, vitreous reflux, syringe design and injection technique. While the IOP elevation is usually short-lived, its magnitude and duration may have clinical relevance, particularly in eyes with pre-existing optic nerve compromise or impaired aqueous outflow.

Previous studies have evaluated post-injection IOP changes following intravitreal administration of agents such as pegaptanib [8], ranibizumab [9], bevacizumab [10] and aflibercept. [11] These studies consistently demonstrate an immediate IOP spike, followed by a rapid decline toward baseline levels. However, reported IOP profiles vary, and direct comparisons between different anti-VEGF agents are limited. Moreover, most available data are derived from heterogeneous study designs or focus on single agents rather than head-to-head comparisons.

Faricimab, a newer bispecific antibody targeting both VEGF-A and angiopoietin-[2,12] has expanded the therapeutic armamentarium for retinal vascular diseases. Alongside faricimab, aflibercept and ranibizumab remain widely used in routine clinical practice. Although large clinical trials have reported isolated cases of transient IOP elevation with these agents, real-world data assessing immediate post-injection IOP behaviour and comparative pressure dynamics remain scarce.

The present study was designed to prospectively evaluate and compare short-term intraocular pressure changes following intravitreal injection of aflibercept 2 mg, ranibizumab and faricimab. By analysing IOP measurements at predefined early time points after injection, this study aims to characterise immediate IOP

responses and determine whether clinically relevant differences exist among these commonly used anti-VEGF agents.

2.Materials and Methods

Study design

This was a prospective, observational, single-centre comparative study conducted at the Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, India.

Study population

Consecutive patients diagnosed with neovascular age-related macular degeneration or diabetic macular oedema and requiring intravitreal anti-VEGF therapy were recruited from the medical retina clinic between November 2025 and January 2026. A total of 75 patients were enrolled and equally allocated into three treatment groups based on the administered intravitreal agent: aflibercept 2 mg (group 1), ranibizumab 0.5 mg (group 2) and faricimab 6 mg (group 3), with 25 patients in each group.

In cases of bilateral disease, only one eye per patient was included to avoid inter-eye correlation. Exclusion criteria included a known diagnosis of glaucoma or ocular hypertension, previous vitreoretinal surgery in the study eye, active ocular infection or inflammation, and inability or refusal to provide informed consent.

At baseline, all participants underwent a comprehensive ophthalmic evaluation, including best-corrected visual acuity assessment, slit-lamp biomicroscopy, fundus examination using indirect ophthalmoscopy, intraocular pressure measurement, and spectral-domain optical coherence tomography, in accordance with standard retinal clinic protocols.

Intravitreal injection technique

All intravitreal injections were administered under aseptic conditions in a dedicated procedure room following institutional protocols. The periocular skin and ocular surface were prepared with 5% povidone–iodine, and a sterile drape and lid speculum were applied in all cases.

Topical anaesthesia was achieved using proparacaine hydrochloride 0.5% eye drops. Intravitreal aflibercept 2 mg (0.05 mL), ranibizumab 0.5 mg (0.05 mL) or faricimab 6 mg (0.05 mL) was injected using a 30-gauge needle. Injections were performed 3.5–4.0 mm posterior to the limbus, depending on lens status, by experienced retina specialists. A sterile cotton-tipped applicator was used at the injection site during needle withdrawal to minimise reflux. Following injection, the ocular surface was irrigated with sterile 0.9% sodium chloride solution, and visual acuity was briefly assessed at the count-fingers level.

Intraocular pressure measurements

Intraocular pressure was measured using a rebound tonometer (iCare IC200, iCare Finland Oy).[13] Six consecutive readings were obtained at each time point, with the device automatically excluding the highest and lowest values and averaging the remaining four readings for analysis. IOP was recorded immediately prior to injection (T0) and at 30 seconds (T1), 5 minutes (T2) and 15 minutes (T3) after injection.

Measurements at T1 were obtained with the patient in a supine position on the procedure table, while measurements at all other time points were taken in the sitting position. All IOP measurements were performed by the same trained examiner, and results were digitally displayed to minimise observer bias.

Outcome measures

Demographic and clinical variables recorded included age, sex, laterality of the treated eye, treatment indication and lens status. The primary outcome measure was the change in intraocular pressure at predefined post-injection time points (T1, T2 and T3) compared with baseline (T0), both within individual treatment groups and between groups. Secondary outcome measures included the incidence of acute post-injection IOP elevation associated with transient visual symptoms requiring intervention.

Statistical analysis

Quantitative variables were summarised as mean with standard deviation or as median with the 25^{th} and 75^{th} percentiles, as appropriate, while categorical variables were expressed as absolute frequencies and corresponding percentages. Intraocular pressure measurements obtained at different time points within each treatment group were analysed using a non-parametric repeated-measures approach. When the overall test indicated statistical significance ($p < 0.05$), post hoc pairwise comparisons with adjustment for multiple testing were carried out.

Comparisons of intraocular pressure between the three treatment groups at corresponding time points were performed using a non-parametric analysis of variance. Where a statistically significant difference was identified, adjusted post hoc analyses were undertaken to account for multiple comparisons. Analysis of intraocular pressure changes according to lens status was not performed, as the study was not powered to detect differences for this variable. All statistical tests were two-tailed, and a p value of less than 0.05 was considered statistically significant. Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA).

3.Results

A total of 75 eyes from 75 patients were included in the study, with 25 patients in each treatment group: intravitreal aflibercept 2 mg (group 1), ranibizumab 0.5 mg (group 2) and faricimab 6 mg (group 3). Baseline demographic and

clinical characteristics of the overall cohort are summarised in Table 1, and intergroup comparisons are shown in Table 2. There were no statistically significant differences among the three groups with respect to age, sex distribution, laterality of the treated eye, indication for treatment (nAMD or DMO), lens status or baseline intraocular pressure.

Table 1: Demographic and baseline characteristics of the study cohort (n = 75)

Variable	Value
Age, median (25^{th}–75^{th} percentile), years	72 (66–78)
Sex: male, n (%)	56 (74.7)
Treatment received	
Aflibercept 2 mg, n (%)	25 (33.3)
Ranibizumab 0.5 mg, n (%)	25 (33.3)
Faricimab 6 mg, n (%)	25 (33.3)
Eye treated: right, n (%)	31 (41.3)
Indication	
nAMD, n (%)	54 (72.0)
DMO, n (%)	21 (28.0)
Lens status: phakic, n (%)	29 (38.7)

AMD, age-related macular degeneration; DMO, diabetic macular oedema.

Table 2: Baseline characteristics according to treatment group

Characteristic	Aflibercept 2 mg (n=25)	Ranibizumab (n=25)	Faricimab (n=25)	P value
Age, median (25^{th}–75^{th}), years	73 (68–79)	71 (65–77)	72 (66–78)	0.62
Baseline IOP, mean ± SD (mm Hg)	13.10 ± 2.60	13.40 ± 2.90	13.80 ± 2.70	0.48
Sex: male, n (%)	19 (76.0)	18 (72.0)	19 (76.0)	0.91
Eye treated: right, n (%)	10 (40.0)	11 (44.0)	10 (40.0)	0.94
Neovascular AMD, n (%)	18 (72.0)	18 (72.0)	18 (72.0)	1.00
Lens status: phakic, n (%)	9 (36.0)	10 (40.0)	10 (40.0)	0.93

AMD, age-related macular degeneration; DMO, diabetic macular oedema; IOP, intraocular pressure.

Intraocular pressure changes within groups

All three treatment groups demonstrated a significant rise in intraocular pressure immediately following intravitreal injection. When compared with baseline IOP (T0), mean IOP values at 30 seconds (T1), 5 minutes (T2) and 15 minutes (T3) were significantly different within each group ($p < 0.001$ for all comparisons).

In the aflibercept group, mean baseline IOP was 13.1 ± 2.6 mm Hg, which increased to 43.4 ± 9.8 mm Hg at T1, followed by a decline to 30.9 ± 8.7 mm Hg at T2 and 20.8 ± 6.1 mm Hg at T3.

In the ranibizumab group, mean IOP increased from 13.4 ± 2.9 mm Hg at baseline to 42.2 ± 10.1 mm Hg at T1, decreasing to 30.2 ± 9.0 mm Hg at T2 and 20.6 ± 6.3 mm Hg at T3.

In the faricimab group, baseline IOP of 13.8 ± 2.7 mm Hg rose to 34.1 ± 8.6 mm Hg at T1, followed by values of 28.7 ± 8.4 mm Hg at T2 and 20.4 ± 5.9 mm Hg at T3.

Comparison of intraocular pressure between groups

Trends in mean IOP across the three groups at different time points are illustrated in Figure 1. At 30 seconds post-injection (T1), the faricimab group demonstrated a significantly lower mean IOP compared with both the aflibercept and ranibizumab groups ($p < 0.05$). No statistically significant difference in mean IOP was observed between the aflibercept and ranibizumab groups at this time point.

At 5 minutes (T2), mean IOP values showed substantial reduction in all groups, and intergroup differences were no longer statistically significant ($p > 0.05$). By 15 minutes post-injection (T3), IOP values had returned to near-baseline levels in all three groups, with no significant differences observed between groups ($p > 0.9$).

Safety

No patient experienced sustained elevation of intraocular pressure or acute visual loss requiring anterior chamber paracentesis during the study period.

4.Discussion

The present study prospectively evaluated early intraocular pressure changes following intravitreal injection of aflibercept 2 mg, ranibizumab and faricimab in a real-world clinical setting. Our findings demonstrate that all three agents are associated with a marked but transient elevation in intraocular pressure immediately after injection, with rapid normalisation within 15 minutes. Importantly, faricimab was associated with a lower immediate IOP spike compared with aflibercept and ranibizumab, while overall short-term IOP behaviour remained comparable across all agents. [7 14 15]

Transient post-injection elevation of IOP following intravitreal anti-VEGF therapy is a well-recognised phenomenon. Several studies have consistently shown an acute rise in IOP within the first minute after injection, followed by a gradual decline toward baseline values over the subsequent minutes. This pressure spike is largely attributed to sudden intravitreal volume expansion and is modulated by ocular rigidity, injection technique, injection speed and reflux at the injection site. In our study, all eyes demonstrated a significant increase in IOP at 30 seconds post-injection, followed by a substantial reduction at 5 minutes and near-baseline values at 15 minutes, consistent with previously published literature.

Table 3: Absolute intraocular pressure values (mm Hg) across time points (mean ± SD; range)

Treatment group	T0 (baseline)	T1 (30 s)	T2 (5 min)	T3 (15 min)
Aflibercept 2 mg	13.10 ± 2.60 (8.0–18.2)	43.40 ± 9.80 (31.5–69.2)*	30.90 ± 8.70 (12.1–45.3)*	20.80 ± 6.10 (10.4–34.8)*
Ranibizumab	13.40 ± 2.90 (9.1–19.0)	42.20 ± 10.10 (30.8–67.5)*	30.20 ± 9.00 (14.0–46.8)*	20.60 ± 6.30 (11.2–35.6)*
Faricimab	13.80 ± 2.70 (9.3–19.4)	34.10 ± 8.60 (21.0–58.9)*	28.70 ± 8.40 (15.8–44.6)*	20.40 ± 5.90 (11.0–33.1)*

*Significant difference ($p<0.001$) for all comparisons within each treatment group. IOP, intraocular pressure; T0, prior to injection; T1, 30 s after injection; T2, 5 min after injection; T3, 15 min after injection.

Among the three agents studied, faricimab demonstrated a significantly lower immediate IOP elevation compared with aflibercept 2 mg and ranibizumab. As all three drugs were administered using an identical injection volume of 0.05 mL and a uniform injection technique, this difference is unlikely to be volume-related. Possible explanations include differences in molecular structure, viscosity, syringe characteristics and injection dynamics[16]. Although ranibizumab and aflibercept showed similar early IOP profiles, both exhibited higher immediate spikes compared with faricimab, suggesting agent-specific biomechanical behaviour within the vitreous cavity.

Despite the statistically significant differences observed at the earliest post-injection time point, intergroup differences were no longer evident at 5 minutes and 15 minutes. By 15 minutes, mean IOP values across all groups had returned to within normal physiological limits. This finding reinforces the transient nature of post-injection IOP elevation and suggests that short-term pressure dynamics are unlikely to have lasting clinical consequences in eyes without pre-existing outflow compromise.[17 18]

Vitreous reflux at the injection site has been proposed as a potential modifier of post-injection IOP. Although reflux was not systematically quantified in the present study, all injections were performed using a uniform technique with a 30-gauge needle by experienced retina specialists, thereby minimising procedural variability. Any influence of reflux would therefore be expected to affect all treatment groups similarly.

No patient in this study developed sustained elevation of IOP or experienced transient visual loss requiring anterior chamber paracentesis. Baseline IOP values in our cohort were within normal limits, which may partly explain the absence of clinically significant adverse events. Eyes with glaucoma or ocular hypertension were excluded; therefore, caution should be exercised when extrapolating these findings to higher-risk populations.[22 23]

The strengths of this study include its prospective design, standardised injection and measurement protocols, and direct head-to-head comparison of commonly used anti-VEGF agents in routine clinical practice. Limitations include the modest sample size and the use of rebound tonometry rather than Goldmann applanation tonometry.[19-21] However, rebound tonometry allowed rapid and position-independent measurements, which was particularly advantageous for immediate post-injection assessment, and has been shown to correlate well with Goldmann measurements.[20]

In conclusion, intravitreal aflibercept 2 mg, ranibizumab and faricimab produce a significant but short-lived increase in intraocular pressure immediately after injection, with normalisation within 15 minutes. Faricimab is associated with a lower early IOP spike, although overall short-term pressure profiles are comparable among the three agents. These findings support the short-term safety of all three drugs and highlight the importance of early post-injection IOP monitoring, particularly in eyes at risk of pressure-related optic nerve damage.

Competing interests

The authors declare that they have no financial or personal relationships with the manufacturers of aflibercept (Eylea®, Bayer), ranibizumab (Lucentis®, Novartis) or faricimab (Vabysmo®, Roche/Genentech) that could have inappropriately influenced the conduct or reporting of this study.

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