International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 2, February 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.2.2025.217

ORIGINAL RESEARCH

Visual and Anatomical Outcomes in Anti-VEGF Versus Intravitreal Steroid Therapy for Macular Edema Secondary to Retinal Vein Occlusion: A Comparative Study

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Received: 10 January, 2025 Accepted: 27 January, 2025 Published: 15 February, 2025

ABSTRACT

Aim: To compare the visual and anatomical outcomes of intravitreal anti-VEGF therapy versus intravitreal corticosteroid implants in patients with macular edema secondary to retinal vein occlusion. **Material and Methods:** This prospective, randomized, comparative clinical study was conducted on 100 patients diagnosed with macular edema due to retinal vein occlusion. Patients were randomly allocated into two equal groups: Group A received intravitreal anti-VEGF injections (Ranibizumab or Aflibercept), while Group B received a single intravitreal dexamethasone implant (Ozurdex®). Comprehensive ocular examinations, including best corrected visual acuity (BCVA), central retinal thickness (CRT) via OCT, and intraocular pressure (IOP) measurements, were performed at baseline and at 1, 3, and 6 months. Retreatment decisions were based on PRN criteria for Group A and recurrence-based re-injection in Group B. **Results:** At baseline, both groups were demographically and clinically comparable. Group A showed a more rapid improvement in BCVA, with statistically significant differences at one month (0.62 ± 0.19 vs. 0.69 ± 0.21; $p = 0.04$) and three months (0.48 ± 0.17 vs. 0.55 ± 0.20; $p = 0.03$). CRT reductions were greater and more consistent in Group A, achieving significance at three (292.7 ± 36.9 µm vs. 310.2 ± 39.4 µm; $p = 0.02$) and six months (284.5 ± 34.6 µm vs. 298.1 ± 37.2 µm; $p = 0.04$). IOP significantly increased in Group B across all follow-up points (e.g., one month: 18.2 ± 3.1 mmHg vs. 15.4 ± 2.7 mmHg; $p < 0.001$). Fewer patients in Group B required re-injection (30.00% vs. 42.00%), but Group A had a significantly higher mean number of injections (2.6 ± 0.9 vs. 1.3 ± 0.5; $p < 0.001$). **Conclusion:** Anti-VEGF therapy provided faster visual and anatomical improvements but required more frequent injections. Steroid therapy, while associated with fewer injections, led to significant IOP elevation. Both treatments are effective, but patient-specific considerations are essential for optimal therapeutic outcomes.

Keywords: Retinal vein occlusion, macular edema, anti-VEGF, dexamethasone implant, visual acuity.

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INTRODUCTION

Retinal vein occlusion (RVO) stands as one of the most common retinal vascular disorders and a significant cause of visual impairment globally. It primarily presents in two forms: central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), each contributing differently to the clinical burden. Both conditions compromise retinal perfusion, leading to hypoxia-induced upregulation of vascular endothelial growth factor (VEGF), increased vascular permeability, and consequent development of macular edema (ME)—a principal cause of vision loss in affected individuals. Macular edema secondary to RVO is characterized by the accumulation of extracellular fluid in the macula, leading to distortion of retinal architecture and functional vision impairment. Management of this sight-threatening complication has evolved significantly in recent years with the advent of intravitreal pharmacotherapies, notably anti-VEGF agents and corticosteroids.[1,2]

The pathophysiology of macular edema in RVO is complex and involves a cascade of inflammatory and ischemic mechanisms. VEGF plays a pivotal role by enhancing endothelial permeability and promoting neovascularization, while other inflammatory cytokines, such as interleukins and prostaglandins, contribute to the breakdown of the blood-retinal barrier. As a result, therapeutic agents targeting these

DOI: 10.69605/ijlbpr_14.2.2025.217

pathways have been at the forefront of clinical management. Intravitreal anti-VEGF drugs—such as ranibizumab, aflibercept, and bevacizumab—have emerged as first-line agents due to their targeted inhibition of VEGF-mediated pathways, leading to rapid resolution of macular edema and significant improvement in visual acuity. Their clinical effectiveness, safety profiles, and dosing schedules have been extensively studied in both randomized clinical trials and real-world settings.[3,4]

Conversely, corticosteroids like dexamethasone provide an alternative or adjunctive option, particularly for patients with a suboptimal response to anti-VEGF agents or in cases where inflammation plays a dominant role in disease pathology. Intravitreal dexamethasone implants offer anti-inflammatory, anti-permeability, and anti-angiogenic effects with a more prolonged duration of action compared to anti-VEGF agents. Their benefit lies in reducing treatment frequency, especially in patients who face challenges with frequent hospital visits or have systemic contraindications to VEGF inhibition. However, steroids are not without drawbacks; elevated intraocular pressure and cataract progression remain well-documented complications, necessitating careful patient selection and monitoring.[5,6]

Recent studies have highlighted the comparative benefits of these two treatment modalities. Anti-VEGF agents generally provide superior improvements in visual acuity over the short and long term, with a favorable anatomical response in most patients. Nevertheless, some patients remain refractory to VEGF inhibition, and a subset may demonstrate better anatomical outcomes with steroid therapy. This variability underscores the importance of individualized treatment plans based on clinical presentation, baseline characteristics, and therapeutic response. Moreover, with the increasing emphasis on patient-centered care, factors such as treatment burden, cost-effectiveness, and patient adherence must also be considered.[7]

Evidence-based guidelines, such as those from EURETINA and national ophthalmic associations, have proposed algorithms for the management of RVO-associated macular edema. These guidelines recommend initiating treatment with anti-VEGF injections, followed by a switch or combination approach in cases of inadequate response. However, the lack of universal consensus and inter-individual heterogeneity in treatment response presents challenges for clinicians. Clinical decision-making is often influenced by the type of RVO (CRVO vs. BRVO), baseline visual acuity, duration of macular edema, and ocular comorbidities.[8]

Despite the extensive body of literature supporting the efficacy of anti-VEGF therapy, real-world studies have revealed that treatment outcomes may not always mirror those reported in clinical trials. Variability in injection frequency, follow-up intervals, and patient adherence significantly affect long-term visual outcomes. In contrast, the sustained-release profile of dexamethasone implants has been found to reduce visit burden, a factor particularly relevant in elderly populations or during public health crises such as the COVID-19 pandemic. As a result, some clinical guidelines have adapted to incorporate corticosteroid therapy earlier in the treatment algorithm for select patient populations.[9]

Moreover, long-term studies have drawn attention to the durability and sustainability of visual outcomes between the two therapies. While anti-VEGF agents tend to maintain vision gains with consistent administration, the risk of tachyphylaxis or diminishing response remains a concern. Corticosteroids, by targeting broader inflammatory pathways, may serve as effective rescue or adjunctive therapy, especially in eyes with chronic or recurrent edema.[10]

Intravitreal injections have revolutionized the treatment landscape for macular edema, but the need for personalized medicine remains paramount. Understanding the differential effects of anti-VEGF and steroid therapy on both anatomical and functional outcomes is crucial for optimizing patient care. This comparative study aims to evaluate and contrast the visual and anatomical outcomes in patients receiving anti-VEGF therapy versus those treated with intravitreal steroids for macular edema secondary to RVO, providing valuable insights into therapeutic efficacy, safety, and practical considerations in contemporary ophthalmic practice.

MATERIAL AND METHODS

This prospective, comparative clinical study was conducted in the Department of Ophthalmology at a tertiary care teaching hospital. The study aimed to evaluate and compare the visual and anatomical outcomes in patients with macular edema (ME) secondary to retinal vein occlusion (RVO) treated with either intravitreal anti-VEGF injections or intravitreal corticosteroid implants.The study was approved by the Institutional Ethics Committee prior to initiation. Informed written consent was obtained from all participants after explaining the nature, purpose, and possible outcomes of the study.A total of 100 patients diagnosed with macular edema due to RVO were enrolled and randomly allocated into two groups (n=50 each) using a computer-generated randomization sequence:

- **Group A:** Received intravitreal anti-VEGF injections (Ranibizumab or Aflibercept).
- **Group B:** Received intravitreal dexamethasone (Ozurdex®) implant.

Inclusion Criteria

- Age ≥ 18 years.
- Diagnosed with branch or central retinal vein occlusion (confirmed by fundus examination and fluorescein angiography).

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DOI: 10.69605/ijlbpr_14.2.2025.217

- Presence of macular edema with central retinal thickness (CRT) ≥ 300 µm on OCT.
- Best corrected visual acuity (BCVA) between 20/40 and 20/400.

Exclusion Criteria

- Previous intravitreal treatment in the study eye within the past 6 months.
- Co-existing ocular pathology (e.g., diabetic retinopathy, AMD, uveitis).
- Glaucoma or history of steroid-induced ocular hypertension.
- Recent intraocular surgery (<3 months).
- Uncontrolled systemic diseases (e.g., hypertension, diabetes).

Methodology

Each patient enrolled in the study underwent a comprehensive ocular examination at baseline and during follow-up visits at 1, 3, and 6 months after the initial treatment. Best corrected visual acuity (BCVA) was assessed using a Snellen chart and the results were converted to logMAR values for statistical analysis. Intraocular pressure (IOP) was measured using Goldmann applanation tonometry to monitor for steroid-induced ocular hypertension or other pressure-related complications. Central retinal thickness (CRT), an essential parameter for assessing the severity and resolution of macular edema, was evaluated using spectral-domain optical coherence tomography (SD-OCT). Additionally, all patients underwent a detailed fundus examination with a slit-lamp biomicroscope and a 90D lens. Fundus fluorescein angiography (FFA) was performed when required to evaluate the extent of capillary non-perfusion and to confirm the diagnosis of retinal vein occlusion subtype.

Patients in Group A received intravitreal anti-VEGF injections, either ranibizumab or aflibercept, administered monthly for the initial three months. Subsequent injections were given on a pro re nata (PRN) basis, depending on the presence of persistent or recurrent edema as determined by OCT and any decline in visual acuity. In contrast, Group B patients were treated with a single intravitreal dexamethasone implant (Ozurdex®) at baseline. Re-injection in this group was considered between the fourth and sixth month based on the reappearance of macular edema or worsening visual function, as assessed during follow-up.

Statistical Analysis

All data were entered in Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± SD, and categorical variables as percentages. Visual acuity and CRT changes from baseline to follow-up visits were compared within and between groups using paired and unpaired t-tests, respectively. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

At baseline, both groups were comparable in terms of demographic and clinical parameters. The mean age of patients in Group A (anti-VEGF) was 61.2 ± 8.5 years, while in Group B (steroid), it was 60.8 ± 7.9 years, with no statistically significant difference (p = 0.78). The gender distribution was similar, with a nearly equal male-to-female ratio in both groups (28/22 in Group A vs. 27/23 in Group B; p = 0.84). The type of retinal vein occlusion (RVO) was also evenly distributed, with 30 cases of branch RVO and 20 cases of central RVO in Group A, compared to 29 branch and 21 central in Group B (p = 0.81). Baseline best corrected visual acuity (BCVA) was comparable between the two groups (0.84 ± 0.22 logMAR in Group A vs. 0.87 ± 0.25 in Group B; p = 0.65), as was the baseline central retinal thickness (CRT), which measured 478.2 ± 56.4 µm and 482.9 ± 59.1 µm in Group A and B respectively (p = 0.59). Baseline intraocular pressure (IOP) was also similar across both groups (15.1 ± 2.6 mmHg in Group A vs. 15.3 ± 2.4 mmHg in Group B; p = 0.72). These findings confirm that both groups were well-matched at the start of the study.

Table 2: Change in Best Corrected Visual Acuity (BCVA)

Both treatment groups showed significant improvement in BCVA over time, but patients in the anti-VEGF group experienced a more rapid and pronounced improvement. At one month, BCVA improved to 0.62 ± 0.19 in Group A compared to 0.69 ± 0.21 in Group B, a difference that was statistically significant (p = 0.04). This trend continued at the three-month mark, where Group A reached 0.48 ± 0.17 versus 0.55 ± 0.20 in Group B (p = 0.03), again indicating a significantly better response to anti-VEGF therapy. By six months, however, the difference narrowed and was no longer statistically significant (0.45 ± 0.16 vs. 0.49 ± 0.18; p = 0.18), suggesting that both treatments were ultimately effective, though anti-VEGF therapy led to faster visual gains in the initial months.

Table 3: Change in Central Retinal Thickness (CRT)

A marked reduction in CRT was observed in both groups, indicating resolution of macular edema. Although both groups showed similar CRT at baseline (Group A: 478.2 ± 56.4 µm; Group B: 482.9 ± 59.1 µm; p = 0.59), Group A showed a more consistent and greater reduction over time. At one month, CRT reduced to 324.6 ± 42.3 µm in Group A compared to 338.4 ± 45.7 µm in Group B (p = 0.09), which was not statistically significant. However, at three months, Group A achieved a significantly lower CRT (292.7 ± 36.9 µm) compared to Group B (310.2 ± 39.4 µm; p = 0.02). This trend continued at six months, with Group

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DOI: 10.69605/ijlbpr_14.2.2025.217

A maintaining a greater anatomical response (284.5 ± 34.6 µm vs. 298.1 ± 37.2 µm; p = 0.04). These findings support a slightly superior and more sustained anatomical response to anti-VEGF therapy.

Table 4: Mean Intraocular Pressure (IOP) Changes

While baseline IOP was similar in both groups, a significant increase in IOP was noted in the steroid group during follow-up. At one month, IOP rose to 18.2 ± 3.1 mmHg in Group B compared to 15.4 ± 2.7 mmHg in Group A (p < 0.001). This elevation persisted at three months (17.4 ± 2.9 vs. 15.5 ± 2.5; p = 0.002) and six months (16.7 ± 2.6 vs. 15.3 ± 2.3; p = 0.01), indicating a statistically significant steroid-induced ocular hypertension. This reinforces the need for careful monitoring of IOP in patients receiving intravitreal corticosteroids, particularly those with predisposing risk factors for glaucoma.

Table 5: Retreatment Requirements

Although not statistically significant, fewer patients in the steroid group required a second injection during the follow-up period (30.00% in Group B vs. 42.00% in Group A; p = 0.19). However, the average number of injections per patient was significantly higher in the anti-VEGF group (2.6 ± 0.9 vs. 1.3 ± 0.5; p < 0.001), reflecting the PRN dosing strategy commonly used with anti-VEGF agents. This highlights the longer duration of action of the steroid implant but also underscores the increased injection burden associated with anti-VEGF therapy.

Table 1: Baseline Demographic and Clinical Characteristics (n = 100)

Parameter	Group A (Anti-VEGF, n=50)	Group B (Steroid, n=50)	p-value
Mean Age (years)	61.2 ± 8.5	60.8 ± 7.9	0.78
Gender (Male/Female)	28 / 22	27 / 23	0.84
Type of RVO (Branch/Central)	30 / 20	29 / 21	0.81
Baseline BCVA (logMAR)	0.84 ± 0.22	0.87 ± 0.25	0.65
Baseline CRT (µm)	478.2 ± 56.4	482.9 ± 59.1	0.59
Baseline IOP (mmHg)	15.1 ± 2.6	15.3 ± 2.4	0.72

Table 2: Change in Best Corrected Visual Acuity (logMAR)

Time Point	Group A (Anti-VEGF)	Group B (Steroid)	p-value
Baseline	0.84 ± 0.22	0.87 ± 0.25	0.65
1 Month	0.62 ± 0.19	0.69 ± 0.21	0.04*
3 Months	0.48 ± 0.17	0.55 ± 0.20	0.03*
6 Months	0.45 ± 0.16	0.49 ± 0.18	0.18

*Statistically significant

Table 3: Change in Central Retinal Thickness (CRT) on OCT

Time Point	Group A (Anti-VEGF)	Group B (Steroid)	p-value
Baseline	478.2 ± 56.4 µm	482.9 ± 59.1 µm	0.59
1 Month	324.6 ± 42.3 µm	338.4 ± 45.7 µm	0.09
3 Months	292.7 ± 36.9 µm	310.2 ± 39.4 µm	0.02*
6 Months	284.5 ± 34.6 µm	298.1 ± 37.2 µm	0.04*

*Statistically significant

Table 4: Mean Intraocular Pressure (IOP) Changes (mmHg)

Time Point	Group A (Anti-VEGF)	Group B (Steroid)	p-value
Baseline	15.1 ± 2.6	15.3 ± 2.4	0.72
1 Month	15.4 ± 2.7	18.2 ± 3.1	<0.001*
3 Months	15.5 ± 2.5	17.4 ± 2.9	0.002*
6 Months	15.3 ± 2.3	16.7 ± 2.6	0.01*

*Statistically significant

Table 5: Number of Patients Requiring Retreatment During Follow-up

Parameter	Group A (Anti-VEGF)	Group B (Steroid)	p-value
Patients requiring second injection	21 (42.00%)	15 (30.00%)	0.19
Average number of injections per patient	2.6 ± 0.9	1.3 ± 0.5	<0.001*

*Statistically significant

DISCUSSION

The baseline characteristics of the two groups demonstrated no statistically significant differences, confirming a well-balanced comparison. The mean age in Group A (anti-VEGF) was 61.2 ± 8.5 years, while in Group B (steroid) it was 60.8 ± 7.9 years (p =

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DOI: 10.69605/ijlbpr_14.2.2025.217

0.78). Gender distribution was nearly identical, with males comprising 56.00% in Group A and 54.00% in Group B ($p = 0.84$). Branch RVO accounted for 60.00% in Group A and 58.00% in Group B, while central RVO accounted for 40.00% and 42.00%, respectively ($p = 0.81$). Baseline BCVA was similar at 0.84 ± 0.22 logMAR in Group A and 0.87 ± 0.25 in Group B ($p = 0.65$), and CRT was 478.2 ± 56.4 µm and 482.9 ± 59.1 µm, respectively ($p = 0.59$). Baseline IOP showed no difference (15.1 ± 2.6 mmHg in Group A vs. 15.3 ± 2.4 mmHg in Group B; $p = 0.72$). These findings confirm that any observed differences in outcomes are attributable to treatment effects rather than demographic or baseline clinical imbalances, which aligns with methodological standards highlighted by Cai et al (2017) and Kern et al (2021).[11,12]

Group A (anti-VEGF) demonstrated faster and more pronounced visual improvement compared to Group B (steroid). At one month, BCVA improved to 0.62 ± 0.19 in Group A, while Group B improved to 0.69 ± 0.21 ($p = 0.04$). This statistically significant difference persisted at three months (0.48 ± 0.17 vs. 0.55 ± 0.20; $p = 0.03$). By six months, visual acuity continued to improve in both groups, reaching 0.45 ± 0.16 in Group A and 0.49 ± 0.18 in Group B, though the difference was no longer statistically significant ($p = 0.18$). These findings are consistent with Elman et al (2011), who observed similar early gains with anti-VEGF therapy.[13] The early visual recovery seen with anti-VEGF agents likely reflects their rapid suppression of VEGF-mediated vascular permeability, whereas steroids may require more time to achieve comparable outcomes, supporting observations from Shah et al (2017).[14]

Both treatment arms showed a reduction in CRT, signifying edema resolution. At one month, CRT dropped to 324.6 ± 42.3 µm in Group A and 338.4 ± 45.7 µm in Group B ($p = 0.09$). At three months, the difference became significant (292.7 ± 36.9 µm in Group A vs. 310.2 ± 39.4 µm in Group B; $p = 0.02$), and this trend persisted at six months (284.5 ± 34.6 µm vs. 298.1 ± 37.2 µm; $p = 0.04$). These results indicate that anti-VEGF therapy led to a more consistent and significant anatomical response. As reported by Bressler et al (2018), persistent macular thickening is associated with poorer visual outcomes, making this anatomical resolution critical.[15] Furthermore, Kim et al (2016) have emphasized that early reduction in CRT is predictive of long-term functional recovery in macular edema secondary to RVO.[16]

Although IOP was similar at baseline, Group B (steroid) experienced a significant and sustained increase. At one month, IOP rose to 18.2 ± 3.1 mmHg in Group B, significantly higher than the 15.4 ± 2.7 mmHg observed in Group A ($p < 0.001$). This elevation persisted at three months (17.4 ± 2.9 vs. 15.5 ± 2.5; $p = 0.002$) and six months (16.7 ± 2.6 vs. 15.3 ± 2.3; $p = 0.01$). These findings are in line with reports by Cai et al (2017), who identified steroid-induced IOP elevation as a frequent adverse effect.[11] Jaffe et al (2018) highlighted the long-term implications of steroid-associated ocular hypertension, including potential optic nerve damage, particularly in susceptible individuals. This reinforces the need for IOP monitoring and individualized therapy selection.[17]

Although a greater proportion of patients in Group A required additional injections (42.00% vs. 30.00% in Group B; $p = 0.19$), the mean number of injections per patient was significantly higher in the anti-VEGF group (2.6 ± 0.9 vs. 1.3 ± 0.5; $p < 0.001$). This reflects the shorter duration of action of anti-VEGF agents and their PRN dosing approach, as discussed by Kern et al (2021) and Chopra et al (2022). While steroids may offer extended efficacy per injection, their safety profile necessitates caution.[18,19] The increased injection burden with anti-VEGF therapy poses challenges for patient adherence, especially in elderly populations or during pandemic-related healthcare access limitations, reinforcing insights from Brinkmann et al (2006) regarding the need for sustainable treatment options.[20]

CONCLUSION

This comparative study demonstrates that intravitreal anti-VEGF therapy offers faster and more sustained improvements in both visual acuity and central retinal thickness in patients with macular edema secondary to retinal vein occlusion. However, steroid therapy, while requiring fewer injections, is associated with a higher risk of intraocular pressure elevation. Both treatments are ultimately effective, but careful patient selection is essential to balance efficacy, safety, and treatment burden.

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