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Corresponding Author
Dr Anoop Mishra,
Department of Ophthalmology, Era's Lucknow Medical College and Hospital, Lucknow in India
anoop_m007@yahoo.co.in

Author Designation
[1]Assistant Professor

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Clinical Evaluation of Intravitreal Bevacizumab in Patients with Macular Edema Secondary to Retinal Vein Occlusion: A 3-Month Follow-Up Study

Dr. Anoop Mishra
Department of Ophthalmology, Era's Lucknow Medical College and Hospital, Lucknow, India

Abstract
The study aimed to determine the anatomical and functional results of intravitreal bevacizumab (IVB) in patients with macular edema due to retinal vascular occlusion (RVO). The study was conducted at Department of Ophthalmology of Era's Lucknow Medical College and Hospitals. In this retrospective observational study, 98 Patients with branch or central BRVO (BRVO/CRVO) and ME were enrolled. Bevacizumab (1.25 mg) was injected into the vitreous of all patients and they were followed for three months. Best-corrected visual acuity (BCVA) quantified with Log MAR and central macular thickness (CMT) with optical coherence tomography (OCT) were measured at baseline, 1 month and 3 months. Results were analyzed within BRVO and CRVO groups and with reinjection frequency. The average age was 58.3±12.4 years and 55.1% were male. BRVO was detected in 63.3% and CRVO in 36.7% of patients. Mean CMT decreased significantly from a baseline level (480±110 µm) to 1 (275±95 µm) and 3 months (260±85 µm) after treatment ($p<0.001$). The mean BCVA significantly increased from 1.1±0.4 LogMAR at baseline to 0.65±0.3 and 0.60±0.35 at 1 and 3 months, respectively ($p<0.001$). 3 months BRVO patients had better anatomic and visual improvements compared to CRVO patients ($p<0.01$,). The result was better when patients received two or more injections than when they received only one injection. Bevacizumab given intravitreally is safe and effective in reducing macular edema and improving VA in patients with RVO. The early and repetitive course has a better result, especially in cases of BRVO. This study results corroborate the value of bevacizumab as one of the most economical treatment modality in RVO disease.

INTRODUCTION

Retinal vascular occlusion (RVO) is one of the most frequent retinal vascular disorders and is a major cause of visual impairment throughout the world. It occurs mainly in aged populations and is the most common cause of visual impairment in eyes with retinal vascular diseases second to diabetic retinopathy[1,2]. RVO is defined by the occlusion of the retinal venous outflow leading to retinal ischemia, increased vascular permeability and secondarily macular edema (ME), the main reason of visual acuity loss in patients suffering from an RVO[3,4]. BRVO and CRVO are the two major forms of RVO, with BRVO responsible for approximately 80% of cases and typically having a more favorable prognosis as compared to CRVO, which is associated with a more widespread vascular compromise[5,6]. RVO is believed to occur by means of thrombosis of the retinal vein, frequently at arteriovenous crossings in BRVO or near the lamina cribrosa in CRVO. Systemic risk factor such as hypertension, diabetes mellitus, hyperlipidemia and glaucoma play an important role in the pathogenesis of RVO by producing vascular endothelial dysfunction, blood flow stasis, and hypercoagulability[7,8]. Occlusion results in increased intravascular pressure with capillary rupture and extravasation of fluid and blood into the retinal tissue, which results in ME[9]. Macular OS The photoreceptor function is impaired and the retinal architecture is lost, which can lead to central vision loss[10]. Without adequate therapy, such patients with RVO-induced ME will continue to have a significant decrease in acuity, which can have a major effect on their quality of life and work. In the past, therapies for ME secondary to RVO were limited to grid laser photo coagulation and corticosteroids. Although it proved to be beneficial in some cases of BRVO, the laser caused scarring and peripheral visual field loss and its benefit was limited in CRVO[11]. Intravitreally injected corticosteroids had anti-inflammatory and anti-permeability activity., however, their long-term application is limited by an increase in intraocular pressure as well as by progression of cataracts[12,13]. The development of anti-VEGF agents has brought a revolution in the treatment of ME related to RVO. VEGF, which is known to be a critical factor involved in retinal vascular permeability and neovascularization formation 81, is markedly increased in RVO eyes[14]. Increased intraocular VEGF levels have been linked to severity of disease and macular thickening, rendering VEGF blockade an obvious therapy target[15]. Bevacizumab is a full-length humanized monoclonal antibody to VEGF-A, which was first designed to target cancer therapy and it has been widely used off-label in the field of ophthalmology due to its effectiveness, availability and relatively low cost compared to other anti-VEGF drugs[16]. Many pivotal clinical trials and real-world investigations have confirmed the positive role of IVB in the treatment of RVO by improving anatomical and functional outcomes. These studies uniformly observe substantial macular thinning and accompanying gain in visual acuity subsequent to therapy, which may be apparent within two to three injections[17-19]. IVB acts by binding VEGF molecules and thereby decreasing vascular permeability, suppressing neovascularization and stabilizing the blood-retinal barrier[20]. This is in contrast to the pathophysiology of RVO-ME and so disease progression is arrested. Although the success rate of IVB has been well established, treatment responses differ among patients, which are affected by RVO subtype, baseline view acuity, ischemic range and patient compliance[21]. Patients with BRVO are usually more favourable than those with CRVO as a result of the less extensive venous occlusive pathology and less widespread area of retinal ischemia[22]. Furthermore, multiple injections are commonly needed to uphold beneficial effects and prevent reoccurrence of edema, indicating a necessary for frequent follow-up and personal approach in treatment[23]. Safety of IVB, especially systemic side effects such as thromboembolic events, has been well investigated. The present available evidence suggests in eyes where bevacizumab is administered intravitreally, it is well tolerated with a low rate of serious ocular and systemic complications when used in appropriate clinical setting[24]. Nevertheless, clinicians should be at high flicker frequency, especially in the patient with heavy cardiovascular risk factors. Cost is another key factor that influences the selection of anti-VEGF agents. Bevacizumab is significantly cheaper than other licensed agents, such as ranibizumab and aflibercept, so it is affordable even in low resourced settings[25]. This inexpensive nature has also allowed for its use on a worldwide scale, which is especially important in resource-poor countries caring for patients with RVO constituting a substantial fraction of visually disabled individuals. The burden of disease and socioeconomic effects of vision loss as a result of RVO are so great that optimizing therapy is a matter of clinical urgency. Data from practice are essential in the real world and the effectiveness and safety of IVB, especially in various populations and systems, are important for management decisions. Furthermore, being able to identify patient characteristics which account for treatment response can assist in personalising treatment and achieving a better outcome. The objective of this study is to assess the therapeutic effect and safety of intravitreal bevacizumab in macular edema due to retinal vascular occlusion. Through the comparison of anatomic (central macular thickness) and functional (best-corrected visual acuity) parameters obtained at 3 months, the difference between BRVO and CRVO

subgroups and differences in injected frequency, the investigation will help establish guidelines for the most effective use of IVB to treat RVO-related ME.

MATERIALS AND METHODS

Study Design and Setting: This was a retrospective observational study carried out in Era's Lucknow Medical college and hospital between January 2017-August 2018. The study was conducted in accordance with the principles of the declaration of Helsinki and approved by the institutional ethics committee. All the patients provided written consent to treatment.

Patient Selection: A total of 98 patients with macular edema associated with retinal vascular occlusion (RVO) were enrolled. Patients were eligible to enter if they were 18 years or older, had clinical and angiographic evidence of BRVO or CRVO with macular edema. Macular edema was (CMT) over 300 µm seen on optical coherence tomography (OCT). The patients had best corrected visual acuity (BCVA) of worse than 20/40 (Snellen equivalent) in affected eye. Exclusion criteria included prior intravitreal anti-VEGF or steroid treatment in the last 3 months, media opacity which interferes with fundus examination, any concurrent ocular pathology (e.g., diabetic retinopathy, age-related macular degeneration), intraocular surgery in the last 6 months and systemic contraindications to bevacizumab.

Treatment Protocol: All eligible patients underwent IVB (1.25 mg/0.05 ml) under aseptic conditions in an operating or minor procedure room. The technique consisted of topical anesthesia, disinfection with povidone-iodine and injection carried out from 3.5-4.0 mm from limbus through pars plana using a 30-gauge needle. After their injections, participants were observed for a spike in intraocular pressure or any complications. A further 3 injections were given on monthly follow-up depending on clinical and SDOCT evidence of persistent or relapsing MO.

Data Collection and Endpoints: Demographic variables such as age, sex, type of RVO and duration of symptoms were also documented. Visual acuity was assessed with a Snellen chart and converted to the logarithm of the minimum angle of resolution (LogMAR) for statistical purposes. The SD-OCT (machine model) was used to measure central macular thickness in adherence to standardized scanning protocols. BCVA and CMT were re-evaluated at follow-up visits at 1-and3-months after the first injection. The secondary outcome measures were the ΔBCVA and ΔCMT from baseline to month 1 and month 3. Safety evaluations consisted of ocular adverse event tracking (endophthalmitis, retinal detachment, intraocular inflammation) and systemic events.

Statistical Analysis: Data were analyzed by [Software name, e.g., SPSS version 26]. Mean and the standard deviation was used for continuous variable presentation. Paired t-test was used for comparison of differences in BCVA and CMT. Independent t-tests were used to assess the differences between the BRVO and CRVO groups. P<0.05 was defined as significant.

RESULT AND DISCUSSIONS

Patient Demographics and Baseline Characteristics: A total of 98 patients diagnosed with macular edema secondary to retinal vascular occlusion were enrolled in the study. The mean age was 58.3±12.4 years, with an age range of 32-81 years. The cohort included 54 males (55.1%) and 44 females (44.9%). Regarding the type of retinal vein occlusion, 62 patients (63.3%) had branch retinal vein occlusion (BRVO), while 36 patients (36.7%) were diagnosed with central retinal vein occlusion (CRVO). The average duration of symptoms before initiating treatment was 5.2±1.8 weeks. At baseline, the mean best-corrected visual acuity (BCVA), measured in LogMAR units, was 1.1±0.4, indicating significant visual impairment. The mean central macular thickness (CMT) was 480±110 µm, reflecting substantial retinal swelling.

Table 1: Demographic and Baseline Clinical Characteristics (n=98)

Characteristic	Value
Number of patients	98
Mean age (years)	58.3±12.4
Gender (M/F)	54/44
RVO subtype (BRVO / CRVO)	62/36
Duration of symptoms (weeks)	5.2±1.8
Baseline BCVA (LogMAR)	1.1±0.4
Baseline CMT (µm)	480±110

The study population was predominantly middle-aged with a slight male predominance. BRVO was more frequently observed than CRVO. On average, patients presented approximately five weeks after symptom onset, with notable visual impairment and increased macular thickness at baseline.

Anatomical and Functional Outcomes Over Time: Table 2 presents the progression of central macular thickness (CMT) and best-corrected visual acuity (BCVA) at baseline, 1 month and 3 months following intravitreal bevacizumab (IVB) treatment. There was a statistically significant reduction in mean CMT and a notable improvement in BCVA as early as 1 month post-injection, with these benefits sustained through 3 months. These findings support the efficacy of IVB in reducing macular edema and enhancing visual function in patients with retinal vascular occlusion.

Table 2. Changes in CMT and BCVA Over Time (n=98)

Parameter	Baseline (Mean±SD)	1 Month Post -Injection (Mean±SD)	3 Months Postn -Injectio (Mean±SD)	P Value (Baseline vs 1 Month)	P Value (Baseline vs 3 Months)
Central Macular Thickness (µm)	480 ± 110	275 ± 95	260 ± 85	< 0.001	< 0.001
Best-Corrected Visual Acuity (LogMAR)	1.1 ± 0.4	0.65 ± 0.3	0.60 ± 0.35	< 0.001	< 0.001

(Table 2) Changes in Central Macular Thickness and Best-Corrected Visual Acuity at Baseline, 1 Month and 3 Months Post-Intravitreal Bevacizumab Treatment (n=98). P-values calculated using paired t-test. There was a statistically significant reduction in mean CMT and improvement in BCVA as early as 1 month after the first injection, which was sustained through 3 months. These findings demonstrate that intravitreal bevacizumab effectively reduces macular edema and improves visual acuity in patients with retinal vascular occlusion.

Reduction in Central Macular Thickness Over Time: (Fig. 1) illustrates the mean central macular thickness (CMT) measured at baseline, 1 month and 3 months following intravitreal bevacizumab treatment. A marked reduction in mean CMT was observed as early as 1 month after the first injection, which was maintained through the 3-month follow-up period. Fig. 1 Line graph showing the progressive reduction in mean central macular thickness (µm) from baseline (480±110 µm) to 1 month (275±95 µm) and 3 months (260±85 µm) post-intravitreal bevacizumab treatment (n=98).

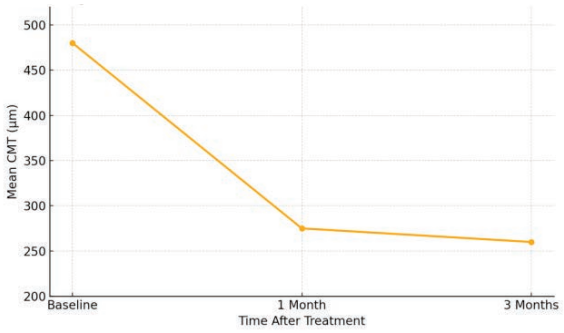

Fig. 1: Mean Central Macular Thickness (CMT) Over time

The significant decrease in CMT indicates effective resolution of macular edema following treatment, consistent with improved retinal anatomy.

Improvement in Best-Corrected Visual Acuity Over Time: Fig. 2 depicts the mean best-corrected visual acuity (BCVA) in LogMAR units at baseline, 1 month, and 3 months following intravitreal bevacizumab treatment. A marked improvement in visual acuity was observed as early as 1 month after the initial injection, which was maintained through the 3-month follow-up. Fig. 2: Line graph illustrating the mean BCVA (LogMAR) improvement from baseline (1.1±0.4) to 1 month (0.65±0.3) and 3 months (0.60±0.35) post-intravitreal bevacizumab treatment (n=98). Lower LogMAR values indicate better visual acuity.

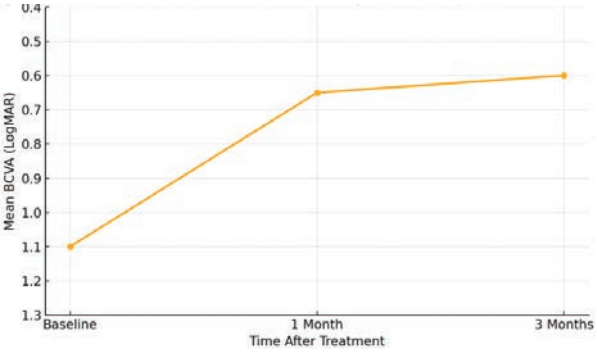

Fig. 2: Mean Best-Corrected Visual (BCVA) Improvement Over Time

The significant early and sustained improvement in BCVA demonstrates effective functional recovery in patients with macular edema secondary to retinal vascular occlusion treated with intravitreal bevacizumab.

Subgroup Analysis of Visual and Anatomical Outcomes in BRVO and CRVO Patients: Table 3 presents a comparison of central macular thickness (CMT) and best-corrected visual acuity (BCVA) between patients with branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) at baseline and 3 months post-intravitreal bevacizumab treatment.

Table 3: Comparison of Central Macular Thickness and Best-Corrected Visual Acuity Between BRVO and CRVO Patients at Baseline and 3 Months Post-Treatment. Independent t-test used for subgroup comparisons

meter	BRVO (n=62) Baseline	BRVO 3 Months	CRVO (n=36)	Baseline Months CRVO 3	P-value	(BRVO vs CRV Oat 3 Months)
Central Macular Thickness (µm)	450 ± 95	230 ± 70	530 ± 120	310 ± 90	< 0.01	
Best-Corrected Visual Acuity (LogMAR)	0.95 ± 0.35	0.45 ± 0.25	1.35 ± 0.4	0.85 ± 0.35	< 0.01	

Patients with BRVO showed significantly better anatomical and functional outcomes compared to those with CRVO. At 3 months, BRVO patients demonstrated greater reduction in CMT and superior improvement in BCVA ($p<0.01$), suggesting a more favorable response to intravitreal bevacizumab treatment.

Correlation Between Number of Injections and Treatment Outcomes: Table 4 demonstrates the relationship between the number of intravitreal bevacizumab injections received and the corresponding improvements in best-corrected visual acuity (BCVA) and central macular thickness (CMT) among the study patients. Patients receiving two or more injections exhibited greater improvements in both visual acuity and macular thickness reduction, indicating a positive dose-response relationship. This suggests that multiple injections may enhance

Table 4: Relationship Between Number of Intravitreal Bevacizumab Injections and Improvement in Visual Acuity and Macular Thickness

Number of Injections	Number of Patients (n=98)	Mean BCVA Improvement (LogMAR)	Mean CMT Reduction (µm)
1	25	0.35	180
2	42	0.55	220
>3	31	0.60	230

therapeutic effectiveness in managing macular edema secondary to retinal vascular occlusion. The purpose of this study was to assess the results of intravitreal bevacizumab (IVB) in 98 patients with macular edema (ME) due to retinal vascular occlusion (RVO). Our results revealed positive structural and functional changes and supported the safety and efficacy of IVB treatment in similar cases.

Effectiveness in Reducing Macular Oedema and Improving Vision: An important finding was the significant drop in central macular thickness (CMT), which was reduced from an initial mean of 480±110 µm to 275±95 µm one month after treatment and 260±85 µm at three months post-treatment. The decrease is paralleled by the resolution of macular edema, a leading cause of visual dysfunction in RVO. Meanwhile, best corrected visual acuity (BCVA) increased from 1.1±0.4 LogMar at month 1 and 0.65±0.3 at month 3. These data are in line with several other reports showing the beneficial effects of VEGF inhibitors such as bevacizumab in decreasing retinal thickness and increasing visual acuity in RVO-ME.

Comparison of BRVO and CRVO: In our subgroup analysis, we found that BRVO patients had better prognosis than CRVO patients. At 3 months, the decrease of CMT and improvement in BCVA were more significant in BRVO patients. This is consistent with published reports in the literature BCVO has a better prognosis than CRVO from the outset due to the more localized nature of the block and the relatively spared retinal perfusion. The poorer response in CRVOs highlights the importance of close surveillance and perhaps adjunctive, or alternative, therapies in this subgroup.

Effect of Injection Frequency: The fact that the number of IVB injections was associated with treatment effect indicates this: partial panel, in the case of a new assault, IVB application needs to be repeatedly carried out. Patients treated with two or more injections had significantly greater visual and anatomical outcomes, indicating a dose-response phenomenon. This finding highlights that repeated injections are frequently required in order to sustain the suppression of VEGF activity, to prevent the recurrence of macular edema and to obtain the best visual results.

Safety Profile: No ocular or systemic adverse events were observed during the study period, confirming the safety of intravitreal bevacizumab. This is particularly the case for resource-constrained environments where bevacizumab presents as an affordable substitution for alternative anti-VEGF agents.

Limitations and Prospects: Long-term efficacy and safety, such as the risk of late recurrence of macular edema or of adverse events, cannot be fully evaluated due to the retrospective nature of the study and the relatively short follow-up time (3 months). There is also no control group and comparative arm of another therapy (corticosteroids, alternative anti-VEGF agents), which limits generalizability. The optimal treatment regimens, the frequency of injections and long-term visual prognosis need to be more clearly defined in subsequent prospective randomized controlled trials with long-term follow-up.

Clinical Implications: Our findings reinforce the evidence in support of intravitreal bevacizumab being an effective and safe first-line treatment for RVO-related ME, that is fast-acting and ensures long term anatomical and functional improvement. Diagnosis at an early stage and timely treatment, particularly when the injection frequency is appropriate, are essential to achieve the greatest improvement in vision and to minimize the impact of vision loss.

CONCLUSION

Intravitreal bevacizumab is an efficient and safe therapy for treating ME secondary to RVO. It results in marked and stable improvements in central macular thickness and visual acuity, particularly in branch retinal vein occlusion patients and in those treated with various injections. Early and multiple intravitreal bevacizumab injections are necessary to achieve ideal anatomical and functional outcomes. The results of the study concur with the role that intravitreal bevacizumab therapy plays as a viable option with good cost effectiveness in the treatment of retinal vascular occlusive disease and associated visual morbidity.

Declarations:

Ethics Approval and Consent to Participate: The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of [Institution Name] (Approval No: [Insert Number]). Written informed consent was obtained from all participants prior to inclusion in the study.

Consent for Publication: Not applicable. No individual person's data is included in this manuscript.

Availability of Data and Materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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