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Original Research Article

EFFICACY OF AS-NEEDED INTRAVITREAL INJECTION COMPARED TO 3-MONTHLY LOADING OF ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR AGENTS FOR BRANCH RETINAL VEIN OCCLUSION

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Abstract: *Branch retinal vein occlusion (BRVO) is a prevalent retinal vascular disorder and a significant cause of vision impairment, particularly in individuals over the age of 50.* ***Objective:*** *The basic aim of the study is to find the efficacy of as-needed intravitreal injection compared to 3-monthly loading of anti-vascular endothelial growth factor agents for branch retinal vein occlusion.* ***Methods:*** *This prospective, comparative study was conducted at Al-Shifa Trust Eye Hospital, Rawalpindi from January 2024 to August 2024. A total of 55 patients diagnosed with BRVO were enrolled in the study.* ***Results:*** *Data were collected from 55 patients with a similar mean age of 53.45 ± 4.56 years and 52.4 ± 7.01 years, respectively. At baseline, the mean best-corrected visual acuity (BCVA) was comparable between the two groups (55.2 in Group A vs. 54.7 in Group B, p = 0.67), as was the mean central retinal thickness (CRT) (485.6 µm in Group A vs. 490.3 µm in Group B, p = 0.73). There were no statistically significant differences between the groups in these baseline characteristics.* ***Conclusion:*** *It is concluded that both the PRN-only and loading phase + PRN regimens are effective for treating BRVO, with the loading phase regimen providing slightly superior visual outcomes.*

Keywords: Intravitreal Injection, Anti-VEGF, Branch Retinal Vein Occlusion, Efficacy, Loading Dose, Retinal Edema

Introduction

Branch retinal vein occlusion (BRVO) is a prevalent retinal vascular disorder and a significant cause of vision impairment, particularly in individuals over the age of 50. It happens when a branch of the retinal vein is obstructed and different complications ensue which bring about macular edema, the gathering of fluids in the macula, and the central vision's hub (1). The most significant cause of vision loss in BRVO is macular edema and, if neglected, could result in irreversible damage to the retinal tissue which IS highly likely to impair the patient's quality of life. Several possibly effective treatment strategies for BRVO have evolved due to the improved knowledge of the condition, particularly macular edema (2). Of these, anti-vascular endothelial growth factor (anti-VEGF) agents have overwhelmingly become the more effective treatment modality. These agents operate by averting the action of the protein component called VEGF which stimulates the unwarranted formation of blood vessels and also causes permeability in the retina resulting in leakage of fluids (3). Since anti-VEGF agents antagonize VEGF activity, they alleviate macular edema and facilitate resolution; a sizable percentage of patients experience visual gain. In patients who underwent BRVO treatment with anti-VEGF, standard therapy is the loading regime, defined as three monthly injections. This is followed by a "pro re nata", (PRN) or as-needed regimen where further injections are given depending on the activity of the disease, on clinical examination and by using imaging such as optical coherence tomography (OCT) (4). The loading phase's purpose is to gain rapid control of macular edema and stabilize the individual's vision and establish this as the platform for the subsequent, PRN phase where additional injections are utilized to maintain these improvements. However, the need for the three-monthly loading phase is still debatable in contemporary discussion. This phase involves regular visits and injections and can be time-consuming, financially demanding to the patient and caregiver, and overburdening to the health care system (5). However, compliance with several injections within the eye lens has several associated complications, including endophthalmitis, intraocular pressure rises, and retinal detachment, though the incidences of these are low (6). As a result, there is an increased effort to find other treatment methods that may minimize the number of injections while maintaining effective therapy (7). Patients are administered with anti-VEGF therapy, but without the monthly injection instead, they are administered with anti-VEGF when features of active macular edema or progression of the disease are observed (8). Advantages of this approach include fewer injections in general, fewer clinic visits and overall costs of treatment. Meanwhile, it may reduce complications related to repeated injections and keep all the therapeutic advantages of anti-VEGF agents (9). Comparing the PRN-only regimen and the standard three-monthly loading followed by PRN is still under study in clinical research. Several reports have proposed that omitting the loading phase may result in less effective visual recovery or less steady control of macular edema which can endanger long-term results (10). However, some other studies have shown that if proper care is taken, and intervention is made early enough, the same vision and structural outcomes can be obtained with less use of the injections. This piece of the debate brings into the limelight the need for an assessment of the two metrics to check if an as-needed-only regimen can offer similar results to the traditional loading phase regimen (11).

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Methodology

The basic aim of the study is to find the efficacy of as-needed intravitreal injection compared to 3-monthly loading of anti-vascular endothelial growth factor agents for branch retinal vein occlusion.

This prospective, comparative study was conducted at Al-Shifa Trust Eye Hospital, Rawalpindi from January 2024 to August 2024. A total of 55 patients diagnosed with BRVO were enrolled in the study.

- Adults aged > 18 years and confirm the diagnosis of BRVO with associated macular oedema confirmed by optical coherence tomography (OCT).
- Best-corrected visual acuity (BCVA) between 20/40 and 20/200 at baseline.
- No previous treatment for BRVO with anti-VEGF agents, laser therapy, or corticosteroids.
- Presence of any other ocular pathology affecting visual acuity, such as age-related macular degeneration, diabetic retinopathy, or significant cataract.
- Active ocular infection or inflammation.

Data collected according to the study was designed as a randomized, interventional trial. Patients were randomly assigned into two groups:

Patients received anti-VEGF injections only on an as-needed basis from the start of the study. Injections were administered when clinical examination and OCT revealed evidence of persistent or recurrent macular edema.

Patients in this group received an initial loading phase consisting of three consecutive monthly intravitreal anti-VEGF injections. Following the loading phase, injections were given on a PRN basis, depending on the presence of macular edema or deterioration in BCVA as detected on follow-up visits.

Both groups received intravitreal injections of a standard anti-VEGF agent: bevacizumab (Avastin) at the clinician's discretion. All of these injections were carried out in the context of an operating theatre by universal precautions given to patients requiring intravitreal injections. One-month follow-up visits were planned for both groups. During these outpatient visits, data were collected from patients for BCVA and images by using OCT.

Data were collected and analyzed using SPSS software v26. Paired t-tests were used to compare changes in BCVA and CRT within groups, while independent t-tests were used to compare differences between the two groups. The chi-square test was employed to compare categorical variables such as the incidence of adverse events. A p-value of less than 0.05 was considered statistically significant.

Results

Data were collected from 55 patients with a similar mean age of 53.45 ± 4.56 years and 52.4 ± 7.01 years, respectively. At baseline, the mean best-corrected visual acuity (BCVA) was comparable between the two groups (55.2 in Group A vs. 54.7 in Group B, p = 0.67), as was the mean central retinal thickness (CRT) (485.6 µm in Group A vs. 490.3 µm in Group B, p = 0.73). There were no statistically significant differences between the groups in these baseline characteristics.

Patients in Group A (PRN-only) experienced a mean BCVA improvement of 9.9 letters, while Group B (Loading + PRN) showed a greater improvement of 13.7 letters, with a statistically significant difference (p = 0.04). Both groups had significant reductions in central retinal thickness (CRT), with Group A showing a reduction of 167.2 µm and Group B a reduction of 184.5 µm, though this difference was not statistically significant (p = 0.11). Importantly, Group A required significantly fewer injections (mean 3.1) compared to Group B (mean 5.7), with a highly significant difference (p < 0.001).

In terms of patient satisfaction, 85% of patients in Group A (PRN-only) reported being "very satisfied" with their treatment, compared to 70% in Group B (Loading + PRN), although this difference was not statistically significant (p = 0.21). Conversely, 15% of patients in Group A and 30% in Group B were "somewhat satisfied," with a similar non-significant p-value (p = 0.21).

Table 1: Baseline Characteristics

Characteristic	Group A (PRN only)	Group B (Loading + PRN)	p-value
Number of Patients	28.0	27.0	-
Mean Age (years)	53.45±4.56	52.4±7.01	-
Mean BCVA (ETDRS letters)	55.2	54.7	0.67
Mean CRT (µm)	485.6	490.3	0.73

Table 2: Combined Visual Acuity, CRT Outcomes, and Number of Injections

Outcome	Group A (PRN only)	Group B (Loading + PRN)	p-value
Mean BCVA Improvement (letters)	9.9	13.7	0.04
Mean CRT Reduction (µm)	167.2	184.5	0.11
Mean Number of Injections	3.1	5.7	<0.001

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Table 3: Patient-Reported Outcomes

Outcome	Group A (PRN only)	Group B (Loading + PRN)	p-value
Very Satisfied (%)	85	70	0.21
Somewhat Satisfied (%)	15	30	0.21

Discussion

This study aimed to compare the efficacy of an as-needed (PRN) intravitreal injection regimen versus the conventional three-monthly loading phase followed by PRN injections in the treatment of branch retinal vein occlusion (BRVO). Nonetheless, the loading phase group of patients showed a more significant gain of BCVA (mean improvement of 13.7 letters) compared to the PRN-only patients (mean improvement, of 9.9 letters) (13). Moreover, this conforms with previous studies that post-loading phase aggression results in faster vision repair in the initial phases of treatment visual gain in the loading phase group, however, while statistically significant there might not be clinically significant improvements for all patients in all cases (14). The additional of about four letters of improvement on the ETDRS chart which is numerically significant may not necessarily be followed by improvement in the patient's daily visual function if the patient has a lesser amount of treatment burden or has co-morbidities. However, there are several principal advantages of the loading phase mentioned in terms of faster and less variable visual outcomes, which should be considered by clinicians when choosing the initial treatment strategy (15). Musculosely, both groups attained a similar reduction of CRT, which is not significantly different between both groups. This implies that control of macular edema is achievable with the PRN-only regimen despite the slight delay in visual acuity rate as compared to the loading phase group. Since visual outcomes in BRVO are strongly associated with macular edema status, this result implies that carefully selected patients might be managed effectively with PRN-only dosing if they prefer less frequent injections to rapid improvement in visual acuity (16). Two important differences between the two groups were the frequency ratio and the number of injections given. Of course, the loading phase + PRN group was given more injections (M=5.7) than the PRN-only group (M=3.1), as hypothesized. It isn't the same clinically, as increased injection frequency is inconvenient for patients and healthcare facilities (17). Repetitive injections raise the probability of Injection-related complications including endophthalmitis, retinal detachment, and elevated intraocular pressure. Furthermore, the difficulties of coming for follow-up visits are a barrier to compliance, particularly among elderly patients with issues with mobility or transport. The attenuation of injection frequency that was observed in the PRN-only group may hold value for subjects who cannot or will not follow a more aggressive dosing schedule (18). However, this burden reduction did not come at the cost of significantly worsening their worst visual acuity or any aspect of the fundus examination, indicating that the PRN-only schedule could be an option for certain patients or those with lower baseline measures of visual loss, or very small or few aggregates (19). Concerning patient-reported measures, satisfaction was reported to be higher in the PRN-only group most probably as a result of willingness to receive fewer injections and consequently visit the clinic less often. Surgeon preference in this study was also consistent with past research where patients are willing to accept slightly worse visual outcomes if the number of injections is decreased (20). The findings in this study imply that the loading phase followed by PRN injections provides a slight edge in terms of visual outcomes than the regimen of PRN-only injection therapy but the patient who wants minimal shots and cheaper treatment can opt for the PRN-only therapy. Clinicians must therefore consider the basic visual calibre of the patient, his commitment to the treatment as well as his preferences while treating BRVO.

Conclusion

It is concluded that both the PRN-only and loading phase + PRN regimens are effective for treating BRVO, with the loading phase regimen providing slightly superior visual outcomes. However, the PRN-only approach significantly reduces the injection burden and treatment costs while maintaining comparable anatomical results, making it a viable option for patients prioritizing fewer interventions.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-JINH-0021/23)
Consent for publication
Approved
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Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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Conception of Study, Development of Research Methodology Design, of manuscript, final approval of manuscript.
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Manuscript drafting.

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