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Original Research Article

To Assess the Effectiveness of Intravitreal Ranibizumab for the Treatment of Macular Edema Associated with Retinal Vein Occlusion (RVO)

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Abstract:

This was a retrospective study of 64 eyes with macular edema associated with RVO. Patients received 0.5 mg of intravitreal ranibizumab (n = 64). Visual acuity, clinical bio-microscopic examination, and central macular thickness (CMT) by Optical Coherence Tomography (OCT) were assessed at 6 weeks post-injection. The CMT before and six weeks after the injection as assessed by OCT were compared. The best-corrected visual acuity significantly improved from the logarithm of the minimal angle of resolution (Logar) 0.851 ± 0.35 at baseline to 0.336 ± 0.20 at 6 weeks (p = 0.001), which is a statistically significant difference. The reduction in CMT was from 524.25± 195.94 µm at baseline to 243±80.72 µm at 6 weeks after receiving intra-vitreal ranibizumab which was also a statistically significant difference (p = 0.001). So, Ranibizumab is effective for the treatment of RVO. The visual outcome and reduction in macular thickness with intravitreal ranibizumab are clinically significant.

Keywords: Retinal vein occlusion, Macular edema, Ranibizumab.

Introduction

Macular edema due to retinal vein occlusion (RVO) is the second most common type of retinal vascular disease after diabetic retinopathy [1] Patients with RVO usually present with progressive diminution of vision mainly due to macular edema [2].

Although branch retinal vein occlusion (BRVO) is the most prevalent type (0.44%) compared to central retinal vein occlusion (CRVO) (0.08%), significant vision loss caused by macular edema secondary to CRVO is more frequent [3]. Recently, anti-vascular endothelial growth factor (VEGF) therapy has become the treatment of choice for this ocular disorder [4].

The Collaborative Branch Vein Occlusion Study (BVOS) reported that grid argon laser photocoagulation was useful in the treatment of macular edema from BRVO. Still, the Central Vein Occlusion Study (CVOS) did not show a similar benefit in CRVO [5]. More recent studies employing intravitreal injection of steroids have shown a benefit in patients with CRVO as well as BRVO [6]. Vascular endothelial growth factor (VEGF) inhibitors have a more favorable safety profile and have been widely used for the treatment of macular edema. Ranibizumab was shown in several randomized prospective trials to be effective and was the first VEGF inhibitor to be FDA-approved for use in RVO [7]. Bevacizumab has also been shown to be effective in multiple trials and is currently being used off-label [8]. In the present study, the effectiveness of ranibizumab in treating retinal vein occlusion with macular edema was observed by comparing the best corrected visual acuity BCVA, and central macular thickness before treatment and after 6 weeks of treatment.

Methodology:

Sample size: Patients with RVO with macular edema attending the outpatient department.

Inclusion criteria:

1. Patients diagnosed with macular edema due to RVO of less than 6 months duration. Both BRVO and CRVO were eligible.

2. CMT greater than 250 μm on spectral domain optical coherence tomography (SD-OCT).
3. BCVA between 0.3 logarithm of the minimal angle of resolution (log MAR) and 1.2 log MAR.

Exclusion criteria

1. Ischemic type
2. No pre-existing glaucoma or ocular hypertension
3. No history of prior laser or intravitreal injections.
4. Presences of any other macular pathology, such as age-related macular degeneration or diabetic retinopathy.
5. Any history of intraocular surgery in the study eye.

Data collection procedure: This was a retrospective observational study where data was collected in pre-designed proforma at the end of the study duration it was analyzed.

The study was approved by the institutional ethical committee. Well-informed and written consent was obtained from the patient.

A total of 64 eyes in 64 patients were included and received ranibizumab for the treatment of macular edema. All patients were examined at baseline, 1st, 3rd, and 6th week after the first treatment. The first examination included a collection of data about the duration of occlusion, previous eye diseases (interventions), existence of other systemic diseases, such as cardiovascular diseases, systemic hypertension, diabetes, thrombosis, and so on.

The ophthalmic examination included the determination of best-corrected visual acuity (BCVA) in Snellen's decimal units (converted to log of the minimum angle of resolution [log MAR] units), intraocular pressure (IOP) measurement by Goldman's applanation tonometer, anterior segment evaluation by slit-lamp bio-microscopy and posterior segment examination with indirect ophthalmoscopy with 20 D lens, description of the type of occlusion (CRVO or BRVO) and the findings of the fundus. The diagnosis was confirmed by fundus fluorescein angiography (FFA) and OCT of the macula (Topcon 3D OCT-2000), whereby the central macular thickness (CMT) was measured in microns. In addition, before the first injection, the following parameters of the general status were determined: differential blood count (platelets), lipid status, blood glucose, and blood pressure. Intravitreal ranibizumab injections were given in the operating room under sterile conditions.

Topical anesthetic drops were given first & then a lid speculum was inserted. The injection site was cleaned with 5% povidone-iodine; 0.5mg (0.05ml) ranibizumab was injected via the pars plana with a 30-gauge needle, 4mm, 3.5 mm and 3 mm away from the limbus in phakic pseudophakic and aphakic patients respectively. The needle was carefully removed using a sterile cotton applicator to prevent reflux. Indirect ophthalmoscopy and tonometry were performed after the procedure to detect any injection-related complications. After the injection, antibiotic eye drops were applied every 6 hours for 1 week.

Result

A total of 64 patients were selected for the study & out of them, 41 were male and 23 were female.

Mean visual acuity was getting better after 6 weeks when compared to before giving intravitreal ranibizumab injection. It was 0.851±0.35 at the time of presentation & 0.336±0.20 after 6 weeks of intravitreal ranibizumab injection. There was a statistically significant difference found in mean visual acuity after intravitreal ranibizumab injection.

We also compare the macular thickness before & after intravitreal ranibizumab injection. There was a statistically significant difference in central macular thickness on comparing with before and after intravitreal ranibizumab injection.

It was 524.25±195.94 before injection, & it decreased to 243.75±80.72. So, there will be a decrease in the central macular thickness after giving the intravitreal ranibizumab injection.

Table 1:

S.N.	Content	Before Intravitreal Injection	After Intravitreal Injection
1.	Visual Acuity	0.851 ± 0.35	0.336 ± 0.20
2.	Central Macular Thickness	524.25 ± 195.94 (Micrometer)	243.75 ± 80.72 (Micrometer)

Discussion

RVO occurs due to blockage of the retinal vein that carries blood away from the retina. Macular edema is the most common and serious complication of RVO, causing vision loss [9].

Currently, treatment of RVO is aimed at reducing macular edema, which is the leading cause of vision loss [10]. Various literature has demonstrated vascular occlusion-related retinal ischemia leading to increased vascular permeability, leakage, neovascularization, and vasodilation in patients with RVO [11,12]. Long-lasting macular edema usually produces secondary retinal pigment epithelial (RPE) changes, which they result in poor visual acuity although various

treatment modalities are available for the treatment of retinal vein occlusion, anti-VEGF agents remain the mainstay of treatment and their efficacy has been demonstrated in various studies. The present study aimed to study the treatment efficacy of Ranibizumab for Macular Edema associated with Retinal Vein Occlusion. The visual acuity improved significantly in patients receiving ranibizumab ($p<0.01$). Ranibizumab decreases macular edema and improves macular function thus improving visual acuity. These findings were in contrast to the findings of Son BK et al in which significant improvement in visual acuity was observed at 6-month follow-up [9]. Qian T et al in their study compared the efficacy and safety of drug therapies (aflibercept, ranibizumab, bevacizumab, pegaptanib, dexamethasone, triamcinolone) for macular edema secondary to central retinal vein occlusion. They observed that only aflibercept and ranibizumab had significantly better efficacy than the sham/placebo group [13]. The BRAVO trial assessed the efficacy of ranibizumab in patients with BRVO and found a significant improvement in visual acuity and a reduction in central foveal thickness in the ranibizumab-treated group compared to a sham group [13].

In a prospective randomized clinical trial by the MARVEL group, the efficacy of IVB and ranibizumab (IVR) in BRVO-ME was compared. The number of injections was not significantly different between the treatment groups (3.2±1.5 versus 3.0±1.4, respectively; $P = 0.55$). There was a significant improvement in VA and CMT in eyes that underwent either bevacizumab or ranibizumab injection without any significant difference between the two drugs [14]. The Central macular thickness represents anatomic changes in the fovea after treatment [16]. Yuan A et al concluded that ranibizumab is associated with improved anatomic results with decreased cystoid macular edema and a trend towards decreased macular thickness, the functional change was not significant as compared to bevacizumab [17].

In the present study, following treatment, a highly significant reduction in CMT was observed amongst the patients receiving intravitreal ranibizumab to CMT reading at presentation ($p<0.01$). Qian T et al reported ranibizumab to be more effective in reducing CRT at 6 months than dexamethasone, and bevacizumab was more effective than triamcinolone but less effective than Ranibizumab [13].Sangroongruangsri S et al could not identify a significant difference in BCVA improvement and CMT reduction among patients treated with Bevacizumab, ranibizumab, and aflibercept [18]. The BRAVO trial assessed the efficacy of ranibizumab in patients with BRVO and found a significant improvement in visual acuity and a reduction in central foveal thickness in the ranibizumab-treated group compared to a sham group [16].

Conclusion

Ranibizumab is effective for the treatment of RVO. The visual outcome and reduction in macular thickness are clinically significant by ranibizumab at the earliest follow-up of 6 weeks.

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