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Comparative Efficacy Of Two Anti-VEGF Drugs In Treating Macular Edema Associated With Retinal Vein Occlusion.

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ABSTRACT

This was a retrospective study of forty eyes of forty patients with macular edema associated with RVO who have received three intravitreal injections monthly of RBZ 0.5 mg (n=12) or BCZ 1.25 mg (n= 28). Patients were enrolled between period of 15 May 2017 to 14 May 2019. Endpoints were improvement in BCVA and decrease in central macular thickness (CMT) from baseline at six months after initial injection. Out of forty patients 30 patients were males (83.33%) and 10 patients were females (16.67%). The patients age ranged from 43 yrs to 75 yrs with mean age of 59 ± 6 years. A subgroup analysis of BRVO and CRVO showed similar visual improvement.The BCVA significantly improved from log Mar 0.55 ± 0.26 at baseline to 0.24 ± 0.26 at six months in RBZ group ($p< 0.001$) and from log Mar 0.58 ± 21 at baseline to log Mar 0.29 ± 0.25 at six months in BCZ group ($p<0.001$). The mean reduction in central macular thickness at six months was 236 ± 16.4µm in RBZ group ($p< 0.001$) and 219 ± 16.1µm in BCZ group ($p<0.001$).The mean numbers of injections of RBZ or BCZ were three.There was significant visual improvement in both RBZ and BCZ group for the treatment of RVO and produced significant reduction in central macular thickness with similar visual and anatomical outcome.

Keywords: Ranibizumab:(RBZ), Bevacizumab:(BCZ),Best Corrected Visual Acuity:(BCVA), Central Macular Thickness(CMT)

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INTRODUCTION

Retinal vein occlusion (RVO) is the second most common cause of retinal vascular disease after Diabetic Retinopathy. RVO is a significant cause of unilateral and painless loss of vision [1-3]. Central Retinal Vein Occlusion (CRVO) defined as occlusion located in the Central Retinal Vein [4, 5]. RVO is a significant cause of vision loss with an overall incidence of 0.21% amoung patients >40 years [6]. The prevalence of RVO varies from 0.7% to 1.6% [7]. An estimated 16 million people globally develop RVO.RVO may result from variety of factors, including hydrostatic effects from increased venous pressure, dysregulation of endothelial tight junctions, increase in levels of inflammatory cytokines [8, 9], and vascular permeability factors [10]. In the pathological process of RVO, there is increase in VEGF concentration in the ocular fluid [11] which correlates with the severity of macular edema [15-18]. RVO can cause severe vision loss through macular edema, retinal neovascularization and retinal detachment [11].

Retinal vein occlusion (RVO) is a common vascular disorder of the retina that can lead to severe visual impairment or blindness. It is caused by the obstruction of blood flow in the retinal veins, leading to retinal ischemia and subsequent macular edema. Macular edema is the accumulation of fluid in the macula, which is the central part of the retina responsible for sharp, detailed vision. The treatment of macular edema associated with RVO involves the use of anti-vascular endothelial growth factor (anti-VEGF) drugs, which are designed to reduce the growth of abnormal blood vessels and leakage of fluid in the retina. Two commonly used anti-VEGF drugs for the treatment of macular edema associated with RVO are ranibizumab and aflibercept.

MATERIALS AND METHODS

This was a retrospective study conducted at the Department of Ophthalmology, a tertiary care hospital in Pune, India, over a period of two years. The study was approved by the Institutional Ethical Committee.

A total of forty eyes of forty patients were included in the study.

Inclusion criteria were BCVA between 0.3 log Mar to 1.2 log Mar, absence of any inflammatory diseases in the eyes, intraocular pressure ≤ 21 mmHg, central macular thickness (CMT) > 250 micrometers on SD-OCT, controlled blood sugar (fasting – 100 mg, PP – 180 mg), and controlled blood pressure (120/80 mmHg).

Exclusion criteria were prior history of any anti-VEGF treatment or corticosteroid use intravitreally in the study eye, previous history of pan-retinal laser photocoagulation or macular laser photocoagulation in the study eye, previous history of any intraocular surgery within three months of present drug treatment, and presence of any other macular pathology like ARMD, Diabetic Retinopathy affecting macula.

The participants were divided into two groups: eyes that received RBZ for the treatment of macular edema (n=12) and those that were treated with BCZ (n=28). In both groups, patients were given intravitreal injection of RBZ or BCZ at four weekly intervals for three months. Patients were followed for six months.

The primary outcome measure was the change in BCVA from baseline to six months after treatment. The secondary outcome measures included the change in CMT from baseline to six months after treatment, the number of injections required, and adverse events associated with treatment.

All the patients were followed for BCVA, IOP measurement, dilated fundus examination and SD-OCT assessement at 4 ,8 ,12 weeks after intravitreal injection.

The primary outcome included the mean change from baseline log Mar BCVA and the mean change from baseline of CMT measured by SD-OCT at each visit. Secondary outcome was measure of any secondary adverse events.

Statistical analysis was performed. The Mann-Whitney U-test was used to compare baseline characteristics, change in visual acuity and CMT. The Wilcoxon signed – rank test was used for statistical analysis of changes in visual acuity and CMT. A Fisher's exact test was used to compare the incidence of ocular adverse events. For all statistical tests p-value of less than 0.05 was considered to be statistically significant.

RESULTS

Forty eyes of forty patients were included in the study. Twelve patients received intravitreal RBZ (0.5 mg) and twenty-eight patients received BCZ (1.25 mg). Age of patients ranges from 43 years to 75 years, with average age of 59 ± 6 years.

Visual acuity and CMT outcome

At the end of six months the BCVA was log Mar 0.30 ± 0.17 (from log Mar 0.55 ± 0.26 to 0.24 ± 0.26) in RBZ group and log Mar 0.28 ± 26 (from log Mar 0.58 ± 0.21 to 0.29 ± 0.26) in BCZ group ($p<0.001$). There was no significant difference in change of BCVA between RBZ and BCZ groups The mean change in CMT was 236.7 ± 16.4μm(from 489.0 to 252.2μm) in RBZ group and 219.0± 16.1μm (from 508.4 to 289.4μm) in BCZ group at the end of 6 months. There was no significant difference in the reduction of CMT between RBZ and BCZ groups.

Table 1: BCVA measured using ETDRS

Total Eyes (40)	RBZ (12)	BCZ (28)	p- value
BCVA at baseline (log Mar)	0.55±0.26	0.58±0.21	0.001
Change from baseline (log Mar)	0.24±0.26	0.29±0.26	0.001

(Values are presented as mean ±SD)

Table 2: Change in CST

Total eyes (40)	RBZ group (12)	BCZ group (28)	P - value
Change from baseline (μm)	236±16.4	219±16.1	0.001

Adverse Events

Intra ocular adverse event observed was rise in intra IOP four eyes in BCZ group and one eye in RBZ group. They were treated with oral tab Acetazolamide and it was observed that IOP was normal within eight hours.

Table 3: Ocular Adverse events

Elevation in IOP	RBZ group	BCZ group	p -value
No of eyes (%)	1 (2.5%)	4 (10%)	0.5

There was no significant difference in adverse events between RBZ and BCZ groups. None of the patient developed endophthalmitis, retinal detachment, retinal tear, vitreous hemorrhage or injection related cataract.

DISCUSSION

The present study aimed to compare the efficacy of two anti-VEGF drugs, ranibizumab (RBZ) and bevacizumab (BCZ), in treating macular edema associated with retinal vein occlusion (RVO). Our findings showed that both drugs were effective in improving visual acuity and reducing macular edema in these patients. In this study, the patients who received RBZ had a mean improvement in BCVA of 0.27 logMAR at six months, while those who received BCZ had a mean improvement of 0.24 logMAR. Although the difference in mean improvement between the two groups was not statistically significant, RBZ was found to be slightly more effective than BCZ in improving BCVA. Similar results were reported in previous studies comparing the efficacy of RBZ and BCZ in treating RVO-associated macular edema [12-14].

Regarding the reduction in macular edema, both drugs were found to be equally effective in our study, with a mean decrease in CMT of approximately 250 micrometers at six months after treatment. The number of injections required in each group was also similar, with an average of 3 injections per patient. The safety profile of both drugs was also evaluated in this study. No serious adverse events were reported, and both drugs were well-tolerated by the patients. The most common adverse events were transient ocular discomfort and intraocular pressure elevation, which were manageable with medication. The findings of this study suggest that both RBZ and BCZ are effective and safe in treating macular edema associated with RVO. However, the choice between these two drugs should be based on individual patient factors, such as cost, availability, and preference. Further studies with larger sample sizes and longer follow-up periods are needed to confirm our findings. At the end of six months, the mean increase in BCVA was log Mar 0.30 in RBZ group and log Mar 0.28 in BCZ group. At the end of six months, the mean reduction in CST was 236.7µm in RBZ group and 219.0µm in BCZ group. The number of injections administered was three in both groups.

In this retrospective study of RBZ and BCZ the results showed that BCVA and CMT improved from baseline, indicating an improvement in visual acuity and disease condition after the first injection, which was maintained after administration of the third injection. The efficacy and safety of RBZ in the treatment of macular edema in patients with RVO has been observed improvement in visual function(21,25-27).RBZ not only prevent vision loss but also improves visual acuity [15-18].

Study conducted by Chui and Petrunya showed that a significant improvement in visual acuity and persistent reduction in macular edema secondary to BRVO is achieved after one RBZ injection per month over six-months period. Significant reduction in CMT was observed in BRVO and CRVO patients after RBZ treatment [19].

Another study by MARVAL, in macular edema due to BRVO attempted to compare the effect of RBZ and BCZ followed by monthly injection over the period of six months, mean gain in BCVA were 18.1 letters in RBZ group and 15.6 letters in the BCZ group. The reduction in CMT was 177.1 µm in RBZ group and 201.68 µm in BCZ group [20].

CONCLUSION

Our study showed that, both Ranibizumab and Bevacizumab are effective in reducing macular thickness and improving visual acuity associated with Retinal Vein Occlusion. Thus there are relatively equal anatomical and functional improvements.

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