

Visual Outcome after Intravitreal Bevacizumab for Macular Edema Secondary to Branch Retinal Vein Occlusion

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Purpose: To determine the effect of intravitreal bevacizumab on visual acuity in patients with macular edema secondary to branch retinal vein occlusion

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Material and methods: This prospective non-randomized clinical interventional study with Convenience (Non Probability) sampling was conducted at Redo Eye Hospital, Rawalpindi; from June 2008 to July 2010. Twenty eyes of twenty patients received a single injection of Bevacizumab in a dose of 1.25 mg/0.05 ml .The visual acuity was measured pre injection and at 4, 8 and 12 weeks post injection using Snellen's visual acuity chart.

Results: At presentation 50% of the patients presented with best corrected visual acuity of 6/60 or worse, 35% were in between 6/60 and 6/24 where as 15 % were 6/18 or better. On the 3rd post injection follow up month 5% of the patients were with best corrected visual acuity of 6/60 or worse , 30 % were in between 6/60 and 6/24 where as 65% were 6/18 or better. The results are statistically significant (p value less than 0.05).

Conclusions: Intravitreal therapy using bevacizumab appears to be an effective treatment for improvement of vision in patients with macular oedema secondary to branch retinal vein occlusion. The positive results though based on short term basis, encourage studies to be conducted on a longer follow up period.

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Branch retinal vein occlusion (BRVO) is a common retinal vascular disease seen most frequently in individuals who are older than 50 years¹. The usual complaint of the patients is sudden loss of vision or visual field defect. The vision is decreased due to complications like macular edema, retinal capillary non-perfusion and vitreous haemorrhage from neovascularisation.

Macular edema is the major cause of visual disturbance in BRVO, occurring in about 60% of cases². Only proven treatment modality for eyes with macular edema secondary to BRVO is macular grid laser photocoagulation. But after grid laser photocoagulation the visual acuity improvement is often very limited (average improvement in vision of 1.33 Snellen's lines)³. It may also be associated with several

complications including sub macular fibrosis, visual-field sensitivity deterioration, enlargement of laser scar and choroidal neovascularisation. This insufficient response to laser therapy has led researchers for other therapeutic options. Several studies have demonstrated the usefulness of intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) agents, such as bevacizumab and ranibizumab in dealing with macular edema due to BRVO^{4,5}. In smaller case series, bevacizumab has been shown to improve visual acuity (VA) and decrease central retinal thickness (CRT) in macular edema secondary due to central retinal vein occlusion⁶.

The purpose of this study was to determine the effect of intravitreal bevacizumab on visual acuity in

patients with macular edema secondary to branch retinal vein occlusion.

MATERIAL AND METHODS

This prospective non-randomized clinical interventional study with Convenience (Non Probability) sampling was conducted at Redo Eye Hospital, Rawalpindi; from June 2008 to July 2010. The patients were first allotted the hospital registration number before proceeding to the examination. Systemic history was taken and general physical examination was done. Complete eye examination was performed including Snellen's best corrected visual acuity (BCVA), intraocular pressure measurement by Goldmann's applanation tonometry, slit-lamp biomicroscopy and indirect ophthalmoscopy.

Twenty patients with acute attack of branch vein occlusion, with duration not more than a month, were selected for the study. We excluded those patients whom best corrected visual acuity was better than 6/12 on initial presentation, who had history of diabetes or nephropathy or previous treatment for BRVO and had other retinal pathologies like glaucoma, diabetic retinopathy and hypertensive retinopathy.

The study procedure and its aim were explained to all the patients before beginning the treatment and they had to sign an informed written consent form.

All intravitreal injections of Bevacizumab (1.25 mg/0.05ml) were performed under topical anesthesia in the operation theatre. Patients used topical antibiotics (moxifloxacin 0.5%, Vigamox Alcon) 4 times per day for 1 week after the injection. The patients were examined after 4, 8 and 12 weeks. On each visit routine evaluation comprising of Snellen's best corrected visual acuity (BCVA), intraocular pressure measurement by Goldmann's applanation tonometry, slit-lamp biomicroscopy and indirect ophthalmoscopy, were done.

All data were analyzed using SPSS 13.0 for windows. The paired t-test was used for comparison of preoperative and post operative BCVA and p value of <0.05 was considered statistically significant.

RESULTS

The study was completed in period of 2 years and a total of 20 eyes of 20 patients (Table 1). At presentation 50% of the patients presented with best corrected visual acuity of 6/60 or worse, 35% were in between

6/60 and 6/24 where as 15 % were 6/18 or better (Table 2).

After one month Post injection 25% of the patients were with best corrected visual acuity of 6/60 or worse , 45% were in between 6/60 and 6/24 where as 30 % were 6/18 or better (Table 2).

Follow up on second Post injection month showed 5% of the patients were with best corrected visual acuity of 6/60 or worse ,35 % were in between 6/60 and 6/24 where as 60 % were 6/18 or better (Table 2).

On the 3rd post injection follow up month 5% of the patients were with best corrected visual acuity of 6/60 or worse , 30 % were in between 6/60 and 6/24 where as 65% were 6/18 or better (Table 2).

There was improvement of at least 2 Snellen's line in visual acuity of all the patients. After comparing the visual acuities at presentation and 3rd month post injection there was statistically significant difference of p value less than 0.05.

Table 1: Gender and age distribution n = 20

Gender	
Male	11 (55%)
Female	9 (45%)
Age (years) Mean \pm SD	57 \pm 1.3

Table 2: Pre and post injection visual acuities n = 20

(BCVA) Visual Acuity	At Pre-sentation	1 st Month Post Injection	2 nd Month Post Injection	3 rd Month Post Injection
6/60 or worse	10	5	1	1
6/60-6/24	7	9	7	6
6/18 or better	3	6	12	13

DISCUSSION

Bevacizumab has been used on "off - label" basis since 2005. Intravitreal bevacizumab was first used by Pai et al⁷ as a treatment for macular edema related to BRVO. The major stimulus for macular edema and neovascularisation seems to be hypoxia-induced production of vascular endothelial growth factor (VEGF), an angiogenic factor that promotes angiogenesis and increases vascular permeability⁴. The

intravitreal bevacizumab has been met with great enthusiasm as an anti VEGF.

Consequently, there have been other reports of short-term beneficial effect of intravitreal bevacizumab to treat macular edema secondary to retinal vascular disease, including central retinal vein occlusion⁶ and diabetic retinopathy⁸. Gunduz⁹ reported a dramatic improvement in the visual acuity with significant macular thickness reduction after intravitreal bevacizumab injections (1.25 mg / 0.05 ml) for patients with BRVO. Jaissle et al¹⁰ demonstrated for the first time a significant long-term effect of intravitreal bevacizumab (1.25 mg / 0.05 ml) for the macular oedema due to BRVO. Their study showed a 39% reduction of the median central retinal thickness and increase of visual acuity to 6/12 at 48 weeks. The result of a prospective clinical trial carried out by Prager et al¹¹ showed that in the BRVO group after intravitreal bevacizumab (1 mg / 0.04 ml) visual acuity increased from 55 ETDRS letters at baseline to 73 ETDRS letters and central retinal thickness decreased significantly after 1 year of follow-up. In our study, we observed significant improvement in visual acuity, 30% of the patients ended up with visual acuity between 6/60 and 6/24 where as 65% with 6/18 or better. All of the patients experienced a significant increase in visual acuity from preoperatively to a final best postoperative visual acuity with improvement of at least 2 Snellen's lines postoperatively.

Some limitations are inherent in our study, such as the small sample size, limited duration of follow-up, non-randomized trial and also as the nature of treatment was prophylactic. The effects of bevacizumab have been reported to be temporary by Gündüz⁹ and Jaissle et al¹⁰. Other reports by Rabena⁴ also disclosed similar results with periods ranging from 2 to 3 months from the last intravitreal bevacizumab to recurrence of macular oedema. Large prospective, randomized clinical trials are necessary to compare the long-term efficacy of intravitreal bevacizumab for patients with macular oedema associated with BRVO.

CONCLUSION

The positive result of this short term study are very encouraging and suggests for a longer randomized study to find out long term efficacy of intravitreal bevacizumab in cases of Branch vein occlusion with macular edema.

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REFERENCE

1. **Martin W, Wilfried R, Iris S, et al.** Role of thrombophilic gene polymorphisms in branch retinal vein occlusion. *Ophthalmology* 2005; 112: 1910-5.
2. **Maurizio BP, Sonela S, Pierluigi I, et al.** Subthreshold grid laser treatment of macular edema secondary to branch retinal vein occlusion with micropulse infrared (810 nanometer) diode laser. *Ophthalmology* 2006; 113: 2237-42.
3. Argon laser photocoagulation for macular edema in branch vein occlusion. The branch vein occlusion study group. *Am J Ophthalmol.* 1984; 98: 271-82.
4. **Rabena MD, Pieramici DJ, Castellarin AA, et al.** Intravitreal bevacizumab (Avastin) in the treatment of macular edema secondary to branch retinal vein occlusion. *Retina* 2007; 27: 419-25.
5. **Campochiaro PA, Heier JS, Feiner L, et al.** Ranibizumab for macular edema following branch retinal vein occlusion: six-month primary end point results of a phase III study. *Ophthalmology* 2010; 117: 1102-12
6. Iturralde D, Spaide RF, Meyerle CB, et al. Intravitreal bevacizumab (avastin) treatment of macular edema in central retinal vein occlusion: a short-term study. *Retina* 2006; 26: 279-84.
7. **Pai SA, Shetty R, Vijayan PB, et al.** Clinical, anatomic and electrophysiologic evaluation following intravitreal bevacizumab for macular edema in retinal vein occlusion. *Am J Ophthalmol.* 2007; 143: 601-6.
8. **Haritoglou C, Kook D, Neubauer A, et al.** Intravitreal bevacizumab (avastin) therapy for persistent diffuse diabetic macular edema. *Retina* 2006; 26: 999-1005.
9. **Gunduz K, Bakri SJ.** Intravitreal bevacizumab for macular edema secondary to branch retinal vein occlusion. *Eye* 2008; 22: 1168-71.
10. **Jaissle GB, Leitritz M, Gelissen F, et al.** One-year results after intravitreal bevacizumab therapy for macular edema secondary to branch retinal vein occlusion. *Graefes Arch Clin Exp Ophthalmol.* 2009; 247: 27-33.
11. **Prager F, Michels S, Kriechbaum K, et al.** Intravitreal bevacizumab (Avastin) for macular oedema secondary to retinal vein occlusion: 12-month results of a prospective clinical trial. *Br J Ophthalmol.* 2009; 93: 452-6.