CHANGES IN MACULAR THICKNESS AND VISUAL ACUITY AFTER INTRAVITREAL BEVACIZUMAB INJECTION IN PATIENTS WITH RETINAL VEIN OCCLUSION

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ABSTRACT

Objective: To evaluate the effect of single Intravitreal Bevacizumab (Avastin) injection on visual acuity (VA) and central retinal thickness (CRT) in patients with macular edema secondary to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

Study Design: Prospective, non-randomized, interventional case series.

Place and Duration of Study: This study was conducted at Al-Shifa Trust Eye Hospital Rawalpindi from March 2012 to February 2013.

Patients and Methods: Twenty three patients with macular edema attributable to vein occlusion received intravitreal injection of Bevacizumab 1.25 mg. Nine patients had central retinal vein occlusion (CRVO) and 14 patients had branch retinal vein occlusion (BRVO). Complete ophthalmic examination including best corrected visual acuity (BCVA) and optical coherence tomography (OCT) was done at base line and follow up visits.

Results: At base line mean visual acuity was Log MAR 0.73 and showed improvement to mean Log MAR 0.39 at 12 weeks after intravitreal Bevacizumab (IVB) injection. Mean CRT was 527 μm at baseline that decreased to 274 μm after 12 weeks of IVB treatment.

Conclusion: Intravitreal Bevacizumab appears to result in significant short term improvement of VA and macular edema secondary to vein occlusion.

Keywords: Bevacizumab flue phrases, BRVO, CRVO, OCT.

INTRODUCTION

Retinal vein occlusion is the second most common retinal vascular disease after diabetic retinopathy and is associated with a severe decrease in visual acuity[1,2]. Decrease in central vision occurs due to persistent macular edema, non-perfusion of parafoveal capillaries and damage to the retinal pigment epithelium attributable to extensive macular hemorrhage[3]. The treatments of the disease remain controversial. Central retinal vein occlusion study group found beneficial effect of laser treatment on neovascularization but failed to produce visual improvement in macular edema. The branch vein occlusion study provided evidence that grid laser photocoagulation of the edematous macular area leads to statistically significant benefits in term of visual acuity and persistence of macular edema as compared to natural course of the disease. However mean improvement in visual acuity was only 1.3 lines but laser treatment lead to the development of scotomas[4].

Several studies have evaluated the efficacy of intravitreal triamcinolone in the treatment of macular edema secondary to both BRVO and CRVO but were only able to show stabilization or only a moderate improvement in visual acuity[5-7]. However the main limitations of intravitreal triamcinolone therapy include high rate of cataract formation or increased intraocular pressure[8].

An alternative for patients with macular edema secondary to retinal vein occlusion is anti-vascular endothelial growth factor (VEGF) therapy. VEGF is a cytokine produced by the hypoxic retina that increases vascular permeability leading to macular edema. VEGF also stimulates endothelial cell hypertrophy that reduces the capillary lumen and causes more ischemia and thus tends to perpetuate the edema[4,9]. Anti-VEGF treatment could break this cycle and facilitate resolution of macular edema. Bevacizumab is a monoclonal antibody that inhibits all isoforms of VEGF. It has been used off-label to treat several ischemic and

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edematous diseases. The purpose of this study was to evaluate the efficacy and safety of intravitreal bevacizumab (IVB) as the sole treatment of retinal vein occlusions presented with decreased visual acuity due to macular edema.

PATIENTS AND METHODS

It was a quasi-experimental study carried out after approval from institutional ethical committee. Twenty-three eyes of 23 patients with macular edema due to retinal vein occlusion with visual acuity equal or less than 6/12 and central macular thickness more than 300 μm were included in this study, Patients previously treated for RVO or with any other ocular disease were excluded from this study.

All patients underwent best corrected visual acuity (BCVA) measurement with Snellen's chart. Visual acuity was converted to logMAR as log of meters on Snellen's chart/6. For example, 6/60 on chart was expressed as log 60/6=1. Slit lamp examination with CRT measurement through fast macular scan using OCT (Stratus OCT Carl Zeiss, USA) was carried out.

Single intravitreal Bevacizumab (Avastin Roche Switzerland) injection of 1.25 mg /0.05 ml was administered to every patient under sterile conditions. Antibiotic and steroid eye drops were prescribed for one week post injection. Patient follow up was performed at, four weeks, and twelve weeks. The BCVA and CRT were measured at every follow up visit.

The statistical analyses were carried out using SPSS version 17.0 (Illinois, USA). Analysis of variance (ANOVA) was applied to asses the changes at 4 and 12 weeks post injection from base line data. Independent sample t-test was applied to compare CRVO group with the BRVO patient group. $p < 0.05$ was considered as significant.

RESULTS

A total 23 eyes of 23 patients were analyzed. Nine patients had CRVO and fourteen patients had BRVO. Fourteen patients (60.86%) were males and nine (39.13%) were females. There were 6 males and 3 females in CRVO group while 8 males and 6 females in BRVO patient group. The mean age was 59.21 years (range from 39 to 81 years). Sixteen patients were hypertensive, two were diabetic, three were both diabetic and hypertensive while in two patients no systemic association was found.

All patients had significant macular edema on OCT (more than 310μm CRT) with BCVA 6/12 or less. None of the patients had undergone any modalities of treatment previously for retinal vein occlusion. At baseline mean BCVA range was 6/12 to 6/180.

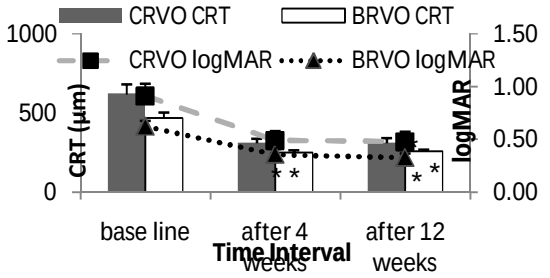
Mean logMAR was 0.73 ± 0.31 (range 0.3 to 1.4) while mean CRT was 527.13 ± 173.08 (range 311 to 890 μm). After 4 weeks of injection the BCVA range was 6/6 to 6/60, mean logMAR 0.41 ± 0.24 (range 0.0-1.0) and mean CRT was 310.33 ± 27.72 (range 194-439 μm). Twelve weeks post injection the BCVA range remained same as 6/6 to 6/60, mean logMAR was 0.39 ± 0.24 (range 0.0-1.0) and mean CRT was 274.70 ± 69.63 (range 148-439 μm).

In CRVO group the range of baseline BCVA was 6/12 to 6/120. The mean LogMAR 0.91 ± 0.36, (range 0.3-1.4) and mean CRT was 617.89 ± 193.41 (range 313-890 μm). After 4 weeks of injection BCVA range was 6/6 to 6/60. Mean logMAR was reduced significantly ($p < 0.022$) to 0.49 ± 0.28 (range 0.0-1.0) from the base line value. The mean CRT was also reduced significantly ($p < 0.0001$) to 310.33 ± 83.17 (194-439 μm) after 4 weeks of injection. Twelve weeks post injection, range of BCVA was 6/6 to 6/60. Mean logMAR was reduced significantly ($p < 0.019$) to 0.48 ± 0.29 (range 0.40-0.0) as compared to the base line value. Mean CRT was also reduced significantly ($p < 0.0001$) to 310.56 ± 94.51 (range 321-490 μm) as compared to base line values (Fig. 1). However, values of logMAR and CRT at week 4 were not significantly different from those at 12 week post injection.

In BRVO group range of BCVA at baseline was 6/12 to 6/60. Mean LogMAR was 0.62 ± 0.21(range 0.3-1.0) and mean CRT was 468.79 ± 36.16 (range 311-677 μm). Mean Log MAR visual acuity was significantly reduced ($p < 0.003$) to 0.36 ± 0.21 (range 0.2-1.0). CRT was also reduced highly significantly ($p < 0.0001$) to

251.79 ± 13.37 (range 148-342 μm). After 12 weeks of injection range of BCVA was 6/7.5 to 6/30, Log MAR visual acuity was significantly reduced ($p < 0.001$) to 0.33 ± 0.17 (range 0.09-0.7) from the base line value. The mean CRT was also reduced significantly ($p < 0.0001$) to 257.36 ± 11.43 (range 205-340 μm) compared to the base line value (Fig.1). The values of logMAR and CRT at 4 weeks post injection did not differ significantly from the values at 12 weeks post injection. The fundus picture and OCT pre and post IVB injection of patient 2 of CRVO group and patient 9 and 4 of BRVO group are shown in fig-2.

The comparison between CRVO to the BRVO group through independent sample t-test showed that the baseline logMAR was significantly higher in CRVO patients ($p< 0.049$) as compared to BRVO patient group. After 4 weeks of injection mean CRT in BRVO patients was significantly reduced compared to CRVO patients ($p<0.046$). Although 12 week post injection no significant difference was observed in the CRT and BCVA of the two patient groups (table). No serious ocular or systemic side effects were noted in any of patients.



*Shows $p < 0.05$ from values at base line

Figure-1: Pre and post injection comparison of CRT and logMAR after IVB in CRVO and BRVO patients.

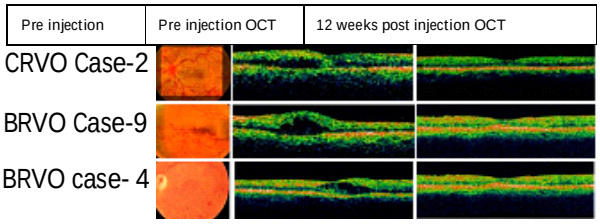


Figure-2: Top row. Pre-injection fundus picture and OCT and Post-injection OCT of case 2 of CRVO group. Middle row, Pre-injection fundus picture and OCT and Post-injection OCT of case 9 of BRVO group. Last row, Pre-injection fundus picture and OCT and Post-injection OCT of case 4 of BRVO group.

DISCUSSION

Use of Bevacizumab in the treatment of various retinal disorders is increasingly being reported[9,10]. Retinal vein occlusion cause visual loss due to initial hypoxia and delayed macular edema. The edema may cause an additional reduction in visual acuity that often exceeds the primary ischaemic damage[11]. It has been shown that intravitreal levels of VEGF are significantly increased after retinal vein occlusions and that the degree of macular edema is correlated with VEGF levels in aqueous humour[12]. In a study with short term follow up Iturralde and associates treated 16 eyes of CRVO with macular edema with intravitreal bevacizumab in which intravitreal corticosteroid therapy had failed, nearly every patient showed anatomical and visual improvement[13]. Spandau and associates also found beneficial effects of intravitreal injection of bevacizumab in a nonischaemic CRVO with macular edema[14].

Table-: Comparison of CRT and logMAR in CRVO and BRVO patients from base line to 4 and 12 week post injection.

Time interval	Parameters	CRVO (n=9)	BRVO (n=14)	Sig.
Base line	CRT (μm)	617.89 ± 193.41	468.79 ± 135.31	0.041
	logMAR	0.91 ± 0.36	0.62 ± 0.21	0.049*↓
After 4 weeks	CRT (μm)	.33 ± 83.17	251.79 ± 50.02	0.046*↓
	logMAR	0.49 ± 0.28	0.36 ± 0.21	0.212
After 12 weeks	CRT (μm)	310.56 ± 94.51	257.36 ± 42.77	0.079
	logMAR	0.48 ± 0.29	0.33 ± 0.17	0.129

*Shows significantly different at $p < 0.05$ compares to CRVO group

The present study shows comparable results with previous reports on intravitreal injection of bevacizumab for macular edema in vein occlusion. It showed marked short-term improvement of vision and reduced macular edema following intravitreal injection of bevacizumab in most of the patients. Some of the patients had recurrence of macular edema with a decreased visual acuity by eight to twelve weeks, it is most likely that eyes receiving early treatment might benefit more than the delayed treatment. Moreover, in case of single intravitreal injection, recurrence of macular edema was the results leading to decreased visual acuity in some patients therefore repeated injections are recommended to sustain the betterment of vision[15]. No systemic side effects were observed and no ocular side effects such as cataract, persistent rise in IOP, vitreous hemorrhage, retinal tear or endophthalmitis were observed in any of the patient that provides evidence of the safety of the treatment. In case of intravitreal triamcinolone acetonide (IVT) used to treat CRVO, increased IOP has been reported, therefore it can be suggested that IVB is a better option than IVT[16].

CONCLUSION

The current study concludes that Bevacizumab administered intravitreally improved visual acuity and macular edema significantly caused by retinal vein occlusion in majority of cases, however in a few number of cases edema recur at 12 weeks. Further larger control trials as well as longer duration of follow up are required to establish the efficacy of intravitreal bevacizumab in resolving macular edema due to retinal vein occlusion.

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