Original Research Article

Efficacy of Intravitreal Bevacizumab for macular edema secondary to Branch retinal vein occlusion

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Received: 2-11-2021 / Revised: 28-12-2021 / Accepted: 07-01-2022

Abstract

Background: Branch retinal vein occlusion is the 2nd most common retinal vascular disease after diabetic retinopathy. The most common cause of visual impairment in BRVO patient is macular edema. **Purpose:** To evaluate the efficacy of Intravitreal injections of Bevacizumab in patients with macular edema secondary to BRVO. **Methods:** All the patients> 18yrs of age with macular edema secondary to BRVO who had treated with Intravitreal Bevacizumab (1.25mg/0.05ml) were analyzed retrospectively. Clinical variables including BCVA, CMT, number of injections and complications were analyzed. **Results:** 23 eyes of 23 patients (11M/12F) were included in study. The mean follow-up period was 5.8±1.7 months. The mean baseline (log MAR) VA was 0.58±0.17 which was significantly improved to 0.36±0.13 at 1 month and 0.33±0.12 at 3 months. The mean CMT at the onset was 355±28.73µm which reduced to 297±28.17µm after 2 weeks of injection and 291±27.13µm at 1 month. Patients had given an average of 2 injections. There were no adverse effects observed following injections. **Conclusion:** It showed a significant reduction in Central macular thickness and improvement in BCVA.

Keywords: Branch retinal vein occlusion, Macular edema, Intravitreal injections, Bevacizumab, Central macular thickness.

Introduction

Branch retinal vein occlusion is the 2nd most common retinal vascular disease after diabetic retinopathy[1]. It's pathogenesis is still not clear but several risk factors have been associated with this disease including hypertension, diabetes mellitus, atherosclerosis, increased BMI, open- angle glaucoma and orbital diseases[2-4].

The most common cause of visual impairment in branch retinal vein occlusion is macular edema. The pathogenesis of macular edema is associated with hypoxia induced production of vascular endothelial growth factor that promotes angiogenesis and increases vascular permeability[5]. Many therapies have been developed for the treatment of retinal vein occlusion. These include surgical intervention, laser therapy, Intravitreal anti VEGF injections and corticosteroids. The mainstay of treatment of macular edema secondary to BRVO is grid laser photocoagulation.[4] Intravitreal anti-VEGF injections are the primary therapy of choice for macular edema in BRVO patients. In 2005, the first report of efficacy of Intravitreal Bevacizumab was given in a BRVO patient having macular edema[6]. Several prospective and retrospective studies showed the beneficial effect of anti VEGF therapy in terms of visual improvement and decrease in central macular thickness in retinal vein occlusion patients having macular edema[7-10]. BVOS study showed that patients having macular edema associated with BRVO with visual acuity of 20/40 or less had significant visual benefit compared with untreated control group[11].

Recently there has been tremendous improvement in Intravitreal anti -VEGF treatment for many ocular diseases such as cystoid macular edema, choroidal neovascularization, coat's disease, retinal neovascularization, radiation induced retinopathy and neovascular glaucoma.In this study we retrospectively analyzed the efficacy of Intravitreal Bevacizumab (Avastin 1.25mg/0.05ml) for patients who had macular edema secondary to BRVO. The main outcome were measured in form of log MAR of best corrected visual acuity and central macular thickness reduction.

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Materials and Methods

This was a Retrospective study done in Regional Institute of Ophthalmology, Rajendra Institute of Medical Sciences, Ranchi between January 2021 to November 2021. This study was conducted in accordance with the tenets of the declaration of Helsinki.

All patients>18 yrs of age with macular edema secondary to Branch retinal vein occlusion were included in the study. Patients with h/o vitrectomy prior to Intravitreal Bevacizumab injection, grid laser photocoagulation, Intravitreal triamcinolone injection, cataract surgery and other surgical procedures were excluded from the study.

Written informed consent was taken from all patients after explaining the procedure. All patients underwent a complete ophthalmic examination which includes BCVA measurement, slit lamp examination, tonometry, dilated fundus examination and optical coherence tomography (stratus OCT Carl Zeiss Meditech). Fluorescein angiography was performed at baseline and at 6 months to identify the presence of BRVO, active extravasation and the extent of retinal non perfusion.

All patients received 1.25mg Intravitreal Bevacizumab (Avastin) in a total volume of 0.05ml. These injections were given under 0.5% Proparacaine anaesthesia in operating room maintaining all aseptic and antiseptic measures. Injection was given through the pars plana route approximately 3.5mm-4mm posterior to the limbus in temporal quadrant directly into vitreous cavity with a 30 gauge needle.

It was given in a slow, steady manner to prevent a sudden flux through the vitreous cavity. Pad and Bandage was done for 4 hours after instillation of Moxifloxacin eye drop. Oral Acetazolamide (250mg) tablet was instructed BD for 2 days to each patient to decrease the chance of IOP rise. Patients were instructed to open their pad and bandage after 4 hours and use eye drop Moxifloxacin 4 times a day for 3 days.

All patients were follow-up on day 1, 3, 7, 14, 30 after that in 2, 3 and 6 months. Complete Ocular Examination including measurement of BCVA, slit lamp examination, IOP, fundus examination was done in each patient. Macular OCT was done on 15days, 1 month, 2months, 3months and 6 months of follow-up for measuring Central Macular Thickness. Those patients whose vision was not improved were given 2nd and 3rd injections in both the groups after 4 weeks and 12 weeks of 1st injection.

Statistical Analysis

All the data were noted on MS Excel sheet and analysed using SPSS 21.0 package (SPSS Inc., Chicago, USA). Differences of Central Macular Thickness between two groups and differences of Best-Corrected Visual Acuity (Snellen visual acuity at 6m was converted into logarithm of minimum angle of resolution log MAR) were calculated with independent t-test. Results of the analysis were evaluated under 95% confidence interval and mean values as mean± SD. The p value <0.05 was considered as statistically significant.

Results

23 eyes of 23 patients (11M/12F) were included in the study. The mean age was 48±5.7 years (range 19-75 years). The mean follow-up period was 5.8±1.7 months.

Females were more in number than males, comprising 52% and 48% of population respectively. The average duration of disease was 2.4 months with a range of 2 wks. to 6 months. The average number of Intravitreal injections given was 2 in number. Accordingly 14 patients were treated with single Intravitreal Bevacizumab injection, 6 patients received two injections and 3 patients received three injections. (Table1)

There were no adverse effects shown following injections in patients.

15 out of 23 patients had superotemporal BRVO, 6 patients had inferotemporal BRVO and 2 patients had macular BRVO. Systemic hypertension was seen in 11(47.8%) cases and 4(17.4%) patients had diabetes mellitus.

The mean best corrected visual acuity at baseline (log MAR) was 0.58±0.17 which was significantly improved to 0.36±0.13 at 1 month, 0.33±0.12 at 3 months and 0.31±0.12 at 6 months. BCVA was improved in 74% of the cases, same in 23% of cases and deteriorated in 3% of cases at 6 months of follow-up.

The mean CMT at the onset was 355±28.73µm which reduced to 297±28.17µm after 2 weeks of injection, 291±27.13µm at 1 month, 267±23.47µm at 3 month and 247±23.15µm at 6 months follow-up.

The mean intraocular pressure after injection was 18.62±1.7 mm of Hg. In 4 eyes intraocular pressure was raised after injection which had controlled with topical and oral anti- glaucoma drugs. The differences between pre injection and post injection status of BCVA, CMT and IOP were shown in (Table 2).

Recurrent macular edema was found in 10.72% of cases at 3 months of follow-up, 33.17% at 6 months of follow-up. Persistent macular edema was present in 2 cases. Among the cases of recurrent macular edema, repeat Intravitreal Bevacizumab was given in 5.8%, combined grid laser and Bevacizumab in 4.5%, only grid laser in 8% and was observed in 6.2% of cases.

Table 1: Baseline Demographic and Clinical characteristics of BRVO Patients

Characteristics	BRVO
Patients	23
Eyes	23
Mean age (in years)	48±5.7
Male: Female	11/12
Duration of disease (months)	2.4
No. of injections(1/2/3)	14/6/3
Diagnosis	
Superotemporal BRVO	15
Inferotemporal	6
Macular	2

*BRVO- Branch retinal vein occlusion

Table 2: Status of BCVA (log MAR), CMT and IOP in patients after successive injections of Intravitreal Bevacizumab

Time	Pre-injection	1 Month	3 Months	6 Months
BCVA(log MAR)±SD	0.58±0.17	0.36±0.13	0.33±0.12	0.31±0.12
Mean CMT(µ)±SD	355±28.73	291±27.13	267±23.47	247±23.15
P Value comparison		<0.001	<0.001	<0.001
Mean IOP±SD	20.13±2.6	18.62±1.7	18.21±1.5	17.93±1.9

*BCVA- Best Corrected Visual Acuity, *CMT- Central Macular Thickness, *IOP- Intraocular pressure, *SD- Standard Deviation

Discussion

The first report on the efficacy of Intravitreal Bevacizumab in a patient with macular edema secondary to retinal vein occlusion came in 2005[12]. After that several studied have been conducted that show a decrease in macular edema and improvement of visual acuity after multiple injections of Bevacizumab but variability in the frequency and outcomes hinder the possibility of comparability of these studies[13-14].

The average number of Intravitreal Bevacizumab injection in this study was 2, ranging from 1 to 3 injections. The average no of

Hikichi et al study reported significant improvement of BCVA un BRVO patients from 0.64±0.24 log MAR units to 0.33±0.21 log MAR units after 1 year, with average 2.6 injections of Bevacizumab in this period. This is comparable to my study where in BCVA improved from 0.58±0.17 log MAR units to 0.31±0.12 log MAR units in the patients of BRVO and an average of 2 injections.[16] The CMT improvement in their study was from 572±134µm injections was less in our study than in the other reported series but it was similar to that of Ahmadi et al[15]. Macular edema assessed by central macular thickness was significantly improved at each visit compared to the baseline values. at baseline to 211±45µm at 1 year. It was slightly better than our results due to the lower number of injections. Hence we consider that the decision for reinjection should be made on the basis of not only the macular thickness but also on visual acuity follow-up.

In our study, there were no any major ocular or systemic problems seen after Intravitreal Bevacizumab, such as retinal detachment, glaucoma, cataract, endophthalmitis or thromboembolic events as reported in other series[17-18].

BERVOLT study showed significant improvement in VA & decrease in CMT with no adverse effect due to IVB injections. Ahmadi et al found that visual outcome was better in non-hypertensive patient, younger patient & pt with better presenting VA but in our study BCVA improved significantly in all patients irrespective of these groups.

Rush et al showed that early diagnosis and treatment of BRVO pts having ME were accompanied by better BCVA and reduced CMT than patients in BRAVO trial.

The limitation of this study was that fundus fluorescein angiography was not performed in all patients at baseline or at follow-up visits to assess the change in capillary non-perfusion areas.

Intravitreal Bevacizumab is a safe and effective drug for reducing macular edema and improving VA as compared to Intravitreal triamcinolone.[19] Intravitreal triamcinolone causes increase in IOP and cataract formation but Intravitreal Bevacizumab has short duration of action and causes recurrent macular edema.

Conclusion

Intravitreal Bevacizumab can be effective and safe drug for reducing macular edema secondary to branch retinal vein occlusion. It shows a significant reduction in CMT and improvement in BCVA. The chances of increase in intraocular pressure and cataract formation are less than Intravitreal triamcinolone.

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Conflict of Interest: Nil Source of support: Nil