Efficacy and Safety of Intravitreal Bevacizumab in Various Retinal Disorders Leading to Macular Edema

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ABSTRACT

AIM
To evaluate the efficacy and safety of intravitreal bevacizumab in macular edema patients.

SETTING
Manjunatha eye hospital, Kundapura, Udupi.

DESIGN
Clinical prospective study.

MATERIALS AND METHODS
A prospective observational study was conducted in 54 eyes of 45 patients between 01/05/2022 to 30/04/2023. All patients belonging to either sex irrespective of age who had macular edema due to various retinal disorders like PDR, CNVM, RVO, CME, VH etc were all included in the study. Patients with tractional retinal detachment, known cases of glaucoma, patients who had thromboembolic episodes like myocardial infarction, stroke in the last 6 months were excluded from the study. All the patients underwent initial ophthalmological examination with visual acuity, refraction, anterior segment examination, intraocular pressure and dilated fundoscopy. OCT was done to all eyes to measure the central macular thickness and correlate post injection. All the patients were given intravitreal injection bevacizumab 1.25 mg/0.05 ml on monthly basis. Patients were followed up 1 week and visual acuity, anterior segment evaluation, IOP, posterior segment examination and OCT were done.

STATISTICAL ANALYSIS
Data was analyzed using descriptive statistics.

RESULTS
A total of 54 eyes of 45 patients were recruited in the study. Out of 45 patients, 18 were males and 27 were females. The age of the patients included in the study ranges from 43 to 79 years. Intravitreal injection was administered 18 in right eyes and 36 left eyes. Among 54 eyes, 29 had PDR, 11 had CNVM, 7 had RVOs, 5 had VH, 2 had post-traumatic CMEs. The mean central macular thickness in PDR was 543 mm, CNVM was 498 mm, RVOs was 457, post-traumatic was 532 mm. After intravitreal bevacizumab, BCVA improved to 6/60-6/24 in 41 eyes, 6/24-6/12 in 13 eyes. At the end of 6 months, BCVA was 6/60-6/24 in 8 eyes, 6/24-6/12 in 27 eyes, 6/12-6/6 in 19 eyes. Central macular thickness also improved to <300 mm in 16 eyes at the end of 6 months.

CONCLUSION
Intravitreal bevacizumab monthly injections in patients with macular edema due to various retinal diseases is safe and effective over 6 months with improvement in BCVA and macular thickness.

KEYWORDS
Intravitreal injection, Bevacizumab, Macular edema, Retinal disorders, Dilated fundoscopy

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INTRODUCTION

Bevacizumab is a full length, humanized monoclonal IgG1 antibody of 149 kDa that targets all biologically active sub types of VEGF A.[1] Even though bevacizumab has not been approved for use in ophthalmological practice, multiple trials have been conducted and proved it to be non-inferior to ranibizumab in terms of safety and efficacy, including the IVAN study, CATT trial, MANT trial, LUCAS trial, and GEFAL trial.[2] As mentioned above, bevacizumab is known to reduce macular edema.[3]

Hence we aimed at studying role of bevacizumab in improving the BCVA and reducing the macular thickness in our patients with various retinal disorders leading to macular edema.[4] Though there are various causes for macular edema we recruited patients who had macular edema occurring mainly as a result of neovascularisation as in proliferative diabetic retinopathy, choroidal neovascular membrane, retinal vein occlusions etc.[5-8]

Objectives of the Study

- To evaluate the efficacy of intravitreal bevacizumab in patients with macular edema due to various retinal disorders.
- To evaluate the safety of intravitreal bevacizumab in patients with macular edema due to various retinal disorders.

MATERIALS AND METHODS

A prospective observational study was conducted in 54 eyes of 45 patients attending the outpatient department of Manjunatha Eye hospital, Kundapura, Udupi.[9] The study period was between 01/05/2022 to 30/04/2023. The patients were included in the study by applying the following Inclusion and Exclusion criteria.[10]

Inclusion Criteria

Patients belonging to either sex irrespective of age who had macular edema due to various retinal disorders like Proliferative Diabetic Retinopathy, clinically significant macular edema, retinal vein occlusions, CMEs, choroidal neovascular membrane who were attending outpatient department of Manjunatha eye hospital were all included in the study.

Exclusion criteria

- Patients with tractional retinal detachment.
- Patients who are known cases of glaucoma.
- Patients who had thromboembolic episodes like myocardial infarction, stroke in the last 6 months.

Methodology

Patients fulfilling inclusion criteria were recruited into this study.[11-15]

The aims and objectives of the intended study was properly explained to the subjects and informed consent was taken. Data was collected as per the proforma sheet.

All the patients underwent initial ophthalmological examination with visual acuity, refraction, anterior segment examination, intraocular pressure and dilated fundoscopy.

Optical coherence topography was done to all eyes to measure the central macular thickness and correlate post injection.

All the patients underwent following systemic examination and blood investigations prior to the procedure:

- Blood pressure test and physician evaluation
- Random blood sugars
- Glycated Hemoglobin (HbA1C)
- HIV
- HBsAg

All the patients were given intravitreal injection bevacizumab 1.25 mg/0.05 ml on monthly basis.

Procedure

Under aseptic precautions, Intravitreal bevacizumab 1.25 mg/0.05 ml injected using a sharp tipped 30-gauge needle after measuring parsplana (4 mm from limbus in phakic/3.5 mm in pseudophakic eyes) in inferotemporal quadrant of the eye under topical anesthesia. Following injection, topical antibiotic was instilled and eye was patched for 2 hours. Oral acetazolamide 250 mg tablet was given to all the patients after the injection. Patients were given topical Gatifloxacin 0.5% with prednisolone acetate combination eye drops 1 drop 2 hourly and then tapered weekly, timolol 0.5% once at night.

Patients were followed up 1 week and visual acuity, anterior segment evaluation, IOP, posterior segment examination were done.

All the patients were given 3 injections on monthly basis. Patients were then followed up at 1 week after every monthly injection, then at 3 months and 6 months. Every follow up, patients underwent following tests- best corrected visual acuity, anterior segment, intraocular pressure measurement and dilated fundoscopy. OCT was repeated at 1month and 3 months follow up.

Data was analyzed using descriptive statistics.

RESULTS

A total of 54 eyes of 45 patients were recruited in the study. Out of 45 patients, 18 were males and 27 were females. The age of the patients included in the study ranges from 43 to 79 years. Intravitreal injection was administered 18 in right eyes and 36 left eyes.

Macular edema due to various disorders were distributed as in Table 1.

Causes	No of eyes
Proliferative diabetic retinopathy with clinically significant macular edema	29
Choroidal neovascular membrane	11
Retinal vein occlusions	7
Vitreous hemorrhage	5
Cystoid macular edema post-traumatic	2
Total	54

Table 1. Macular Edema Due to Various Disorders Were Distributed.

Pre-intravitreal bevacizumab, BCVA and central macular thickness is distributed as in Table 2 (Figure 1).

Causes	Mean BCVA (Snellen's)	Mean CMT(mm) (Range)
Proliferative diabetic retinopathy with clinically significant macular edema	CF 1 mtr	543 (482 mm- 776 mm)
Choroidal neovascular membrane	6/60	498 (445 mm-684 mm)
Retinal vein occlusions	3/60	457 (432 mm-574 mm)
Vitreous hemorrhage	Hand movements	
Cystoid macular edema post-traumatic	6/60	532 (513 mm-551 mm)

Table 2. Pre-intravitreal Bevacizumab, BCVA and Central Macular Thickness is Distributed.

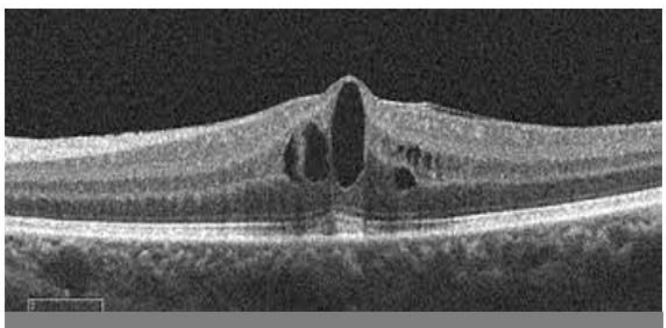

Figure 1. Pre-intravitreal Bevacizumab, BCVA and Central Macular Thickness.

Post injection at 1 week, BCVA is t abulated in Table 3.

Causes\BCVA	6/60-6/24	6/24-6/12	6/12-6/6
Proliferative diabetic retinopathy with clinically significant macular edema	21	8	0
Choroidal neovascular membrane	9	2	0
Retinal vein occlusions	6	1	0
Vitreous hemorrhage	3	2	0
Cystoid macular edema post-traumatic	2		0
Total	41 (75.92%)	13 (24.07%)	0

Table 3. Post Injection at 1 Week, BCVA is Tabulated.

Post injection at 6 months, BCVA as follows (Table 4).

Causes\BCVA	6/60-6/24	6/24-6/12	6/12-6/6
Proliferative diabetic retinopathy with clinically significant macular edema	6	18	5
Choroidal neovascular membrane	2	8	1
Retinal vein occlusions	0	0	7
Vitreous hemorrhage	0	0	5
Cystoid macular edema post-traumatic		1	1
Total	8 (14.81%)	27 (50%)	19 (35.18%)

Table 4. Post Injection at 6 months, BCVA as Follows.

Central macular thickness at 1-week post injection as in Table 5.

Causes\BCVA	>450mm	301 mm-450 mm	<300 mm
Proliferative diabetic retinopathy with Clinically significant macular edema	22	8	0
Choroidal neovascular membrane	9	2	0
Retinal vein occlusions	6	1	0
Vitreous hemorrhage	3	2	0
Cystoid macular edema post-traumatic	2		0
Total	42	13	0

Table 5. Central Macular Thickness at 1 Week Post Injection.

Central macular thickness at 6 months as in Table 6 (Figure 2).

Causes\CMT	>450 mm	301 mm-450 mm	<300 mm
Proliferative diabetic retinopathy with Clinically significant macular edema	6	18	5
Choroidal neovascular membrane	2	8	1
Retinal vein occlusions	0	3	4
Vitreous hemorrhage	0		5
Cystoid macular edema post-traumatic	0	1	1
Total	8	30	16

Table 6. Central Macular Thickness at 6 Months.

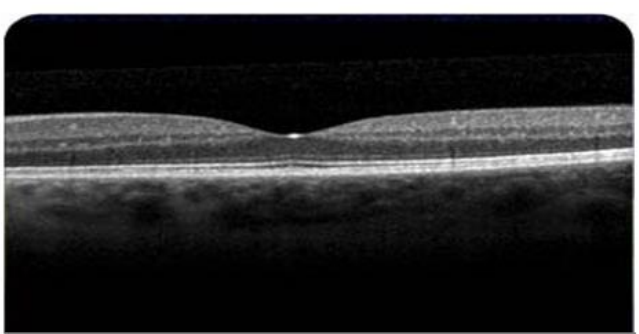

Figure 2. Central Macular Thickness at 6 months.

DISCUSSION

VEGF plays a key role in the pathogenesis of DME. Several reviews have been conducted on the efficacy of the two anti-VEGFs, bevacizumab and ranibizumab, in the treatment of DME. Bevacizumab is a full-length humanized antibody that binds all types of VEGF-A. It is approved by the Food and Drug Administration for the treatment of various cancers, but it is used off-label intravitreally to treat ocular diseases, including proliferative diabetic retinopathy and DME. Despite their widespread clinical applications, the pharmacokinetics of intravitreal bevacizumab concerning untreated eyes has not been extensively studied. There is a systemic penetration of bevacizumab from human eye injections, and it is demonstrated that there is a significant reduction in plasma VEGF after an intravitreal injection with bevacizumab but not ranibizumab. In contrast to ranibizumab, the intravitreal administration of bevacizumab resulted in a statistically significant decrease in the macular thickness of the untreated eye in patients with bilateral DME.

Our study also proved significant improvement in visual acuity in 75% of patient to better than 6/60 and by the end of 6months 85.2% of the patients had BCVA better than 6/18. Remaining patients had cataract in the effected eyes. They underwent phacoemulsification with foldable IOL implantation under local anesthesia after 8-12 months. All the patients had BCVA better than 6/12. 2 patients with PDR had recurrence and aggravation of macular edema following cataract extraction. They undertook a repeat intravitreal bevacizumab injection 4weeks post phacoemulsification. None of the patients had any IOP surge or any other serious adverse effects like vitreous hemorrhage, retinal detachment, endophthalmitis etc.

CONCLUSION

Intravitreal bevacizumab is a safer and cost effective option in patients with macular edema. Bevacizumab monthly injections in patients with macular edema due to various retinal diseases is effective with improvement in best corrected visual acuity and reduces macular thickness.

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