Original Article

Effect of intravitreal bevacizumab injection on visual acuity in patients with proliferative diabetic retinopathy

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ABSTRACT

Objective: To determine the effect of intravitreal bevacizumab injection on visual acuity in patients with proliferative diabetic retinopathy.

Methodology: Seventy eyes of 52 patients of proliferative diabetic retinopathy with visual acuity of ≤6/36 were selected from 26-02-2009 to 25-08-2009, at Retina Clinic of Layton Rehmatulla Benevolent Trust Eye and Cancer Hospital, Lahore, for this case series study. After taking aseptic measures intravitreal (1.25mg/0.05ml) Bevacizumab injection was injected. Post injection follow up was done for best corrected visual acuity with snellen visual acuity chart on 1st week, 6th week and 12th week. Efficacy was considered as gain of one or more snellen visual acuity chart line after 12 weeks. Effect modifiers like age and duration of diabetes mellitus (≤10 years, >10 years) were addressed through stratification.

Results: The mean±Standard Deviation (SD) of patients' age was 47.2±7.9 years. Females 42 (60%) outnumbered the males. Majority of patients 38 (54.3%) had diabetes for more than 10 years. Overall improvement rate was 11 (15.7%) with significant improvement from 1.028 log MAR at baseline to 0.99 at 12 weeks (Paired t test p=0.0014, 95% Confidence interval of mean difference=0.016-0.062).

Conclusion: Intravitreal bevacizumab injection is effective in patients of proliferative diabetic retinopathy for short term results.

KEY WORDS: Efficacy, Intravitreal bevacizumab, Proliferative diabetic retinopathy, Visual acuity.

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INTRODUCTION

Diabetes Mellitus has a complication, i.e. diabetic retinopathy that cause a threat to eye sight of the people in developed and developing countries like Pakistan.[1] Majority of the adults became blind due to proliferative diabetic retinopathy (PDR) and predominantly treated by pars plana vitrectomy and Argon laser but the risk of complication due to the bleeding from fibrovascular membrane (FVM) is still a sign of concern.[2-4] A humanized vascular endothelial growth factor (VEGF) antibody named Bevacizumab (Avastin Genetech Inc, South San Francisco, California, USA) used for metastatic colorectal carcinoma but recent reports have proved its efficacy in the treatment of ocular neovascular

disorder, i.e. proliferative diabetic retinopathy.[5-9] Adjunctive use of intravitreal Bevacizumab before pars plana vitrectomy for severe PDR has also been done and reported by some.[6,7]

This study was conducted to find out the effect of intravitreal bevacizumab injection on visual acuity in patients with proliferative diabetic retinopathy.

METHODOLOGY

This descriptive case series study was conducted at Retina Clinic of Layton Rehmatulla Benevolent Trust Eye and Cancer Hospital, Lahore from 26th February 2009 to 25th August 2009. The calculated sample size is 70 cases, with 95% confidence level, 5% margin of error, taking expected percentage of improvement in best corrected visual acuity by intravitreal bevacizumab injection, i.e. 17.9%.

Sampling Technique: Non-probability purposive sampling.

Inclusion Criteria:

1. Age 30-60 years irrespective of duration of diabetes.
2. Both genders (male and female)
3. Visual acuity ≤6/36
4. New vessels at disc or new vessels elsewhere at fundus with or without vitreous hemorrhage due to proliferative diabetic retinopathy.
5. Phakic eyes.

Exclusion Criteria:

1. History of ocular trauma or ocular surgery.
2. Retinal detachment on slit lamp examination with 90D.
3. Cataract on slit lamp examination.
4. Glaucoma on slit lamp examination
5. Ocular vascular diseases other than diabetics.

Efficacy: The change in best-corrected visual acuity (BCVA) measured by snellen visual acuity chart and graded as improvement (gain of one or more snellen visual acuity chart line), static (no change in visual acuity), worsen (loss of one or more snellen visual acuity chart line) 12 weeks after intravitreal bevacizumab injection. Efficacy was considered and measured if there was overall improvement after 12 weeks.

Procedure: A total of 70 eyes of 52 diagnosed patients of proliferative diabetic retinopathy who fulfilled the inclusion criteria were taken from outdoor of said hospital. The data was collected through a pre-designed proforma comprised of two portions. First portion contained sociodemographic information (name, age, gender) was taken at the time of recruitment. Second portion contained study variable (best corrected visual acuity) that were recorded by snellen visual acuity chart post intravitreal bevacizumab injection.

After taking aseptic measures, study eyes received one single injection of 1.25 mg (0.05 ml) bevacizumab (Avastin; Genentech, Inc., South San Francisco, CA, USA) into the vitreous cavity via pars plana 4mm superotemporal from the limbus; 14 eyes required a second injection for angiographic neovascular leakage 12-24 weeks after the first injection under local anesthesia with lignocaine. Post injection follow up was done for BCVA and any complication, i.e. conjunctivitis, subconjunctival haemorrhage, retinal detachment, endophthalmitis or vitritis. BCVA was checked with snellen visual acuity chart on 1st week, 6th week and 12th week. Effect modifiers like age and duration of diabetes mellitus (≤10 years, >10 years) were addressed through stratification. The main outcome measure was BCVA score.

Statistical Analysis: Data were subjected to analysis by SPSS version 16 (SPSS Inc., Chicago, IL, USA). Descriptive analysis for continuous variable was done as mean±standard deviation (SD), while categorical data were presented as frequency and percentage. Modified Wald method was also used to identify the 99% confidence interval (CI) of proportion. Paired t test was used to measure the difference between continuous variables, i.e. pre and post-injection logMAR values. A p value < 0.05 was considered to be significant.

Ethical Issues: This study was approved by local ethics committee of the hospital. Written informed consent was taken from each subject after they made aware of study in detail.

RESULTS

The mean age + standard deviation (SD) of the patients was 47.2±7.9 years. Age group of 41-50 years had majority of subjects 32 (45.7%) as well as improvement rate 6 (8.6%). Females 42 (60%) outnumbered the males. Majority of subjects 8(11.4%) improved with diabetes mellitus up to 10 years. Table-I

No eye developed any complication except two who developed subconjunctival haemorrhage supratemporally at the entry site of injection, which was completely resolved on 6 week follow up visit. After one week of injection the BCVA of only one patient was improved, but after six weeks improvement reached up to 5 (7.1%). Overall improvement rate was 11 (15.7%). The bevacizumab treatment resulted in a significant improvement from 1.028 log MAR at baseline to 0.99 at 12 weeks

Table-I: Subjects improvement with regards to age and diabetes mellitus history (N=70).

	*Improved**	*Static Not-improved**	*Total**
Age Groups (Years)	n(%)	n(%)	n(%)
30-40	1(1.4)	15(21.4)	16(22.9)
41-50	6(8.6)	26(37.1)	32(45.7)
51-60	4(5.7)	18(25.7)	22(31.4)
Total	11(15.7)	59(84.3)	70(100)
Diabetic history			
≤10 years	8(11.4)	24(34.3)	32(45.7)
>10 years	3(4.3)	35(50.0)	38(54.3)
Total	11(15.7)	59(84.3)	70(100)

*% has been calculated from n=70.

(Paired t test p=0.0014, 95%Confidence interval of mean difference=0.016-0.062). Table-II, Fig. 1

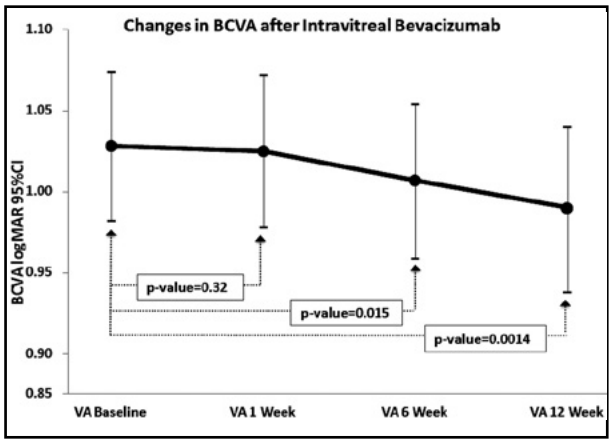

Fig-1: Changes in best-corrected visual acuity (BCVA) after intravitreal bevacizumab.

BCVA improved at 6-weeks from mean logMAR = 1.028 to mean logMAR = 1.007, a difference that was statistically significant (p = 0.015), that further improved at 12-week up to mean logMAR = 0.99 (P = 0.0014).

DISCUSSION

A few studies conducted in Pakistan about the efficacy of intravitreal bevacizumab injection in the management of proliferative diabetic retinopathy (PDR) have reported improving visual acuity, diabetic macular edema (DME), and retinopathy of prematurity. Studies have also been done to highlight the side effects of this drug. A quasi-experimental study was conducted on 150 eyes of 102 patients in Karachi, Pakistan about the efficacy of this drug on PDR. It was found that 90(60%) eyes showed total regression of neovascularization (RNV) while remaining had partial or no RNV. On the other hand BCVA of the subjects showed improvement with no significant side effects.[10]

Another prospective interventional case series study was carried out in Karachi, Pakistan on 24 eyes to describe the effect of intravitreal bevacizumab on visual acuity and central macular thickness in patients with DME who were already treated with macular laser photocoagulation. The improvement in BCVA was found to be 0.90±0.22 (p=<0.0001) and 0.94±0.20 logMAR (p=0.001) at one month and three months interval, respectively while the mean baseline BCVA was of the study eyes was 1.033±0.16 logMAR.[11]

A randomized controlled trial on parallel group study of 60 eyes of 60 patients, having diabetic macular edema and lens opacity was conducted in Karachi, Pakistan to evaluate the efficacy of a single intravitreal Bevacizumab injection after or during cataract surgery for the management of postoperative vision decline in patients with DME. Mean changes in BCVA at 6 weeks was compared with the baseline and it was found that there were a worsening of visual acuity in the control group that was given no injection and an improvement of visual acuity in the Bevacizumab group (p = 0.01).[12] Mean age of patients in our study was 47.2±7.9 years while other study had 54.7±10.1 years[13], While females outnumbered the males was consistent with the study of Mirshahi.[14] We found post injection improvement in visual acuity in 15.7%

Table-II: Effect of intravitreal bevacizumab injection on visual acuity (N=70).

	Pre-injection	*1 week Post-injection*	*6 week Post-injection*	*12 week Post-injection*	*Pre-injection*	*12 week*
Visual Acuity	n(%)	n(%)	n(%)	n(%)	99%CI	99%CI
6/12	0	0	0	1(1.4)	0-0.1	0.0-0.12
6/18	0	0	1(1.4)	0	0-0.1	0-0.1
6/24	0	1(1.4)	0	1(1.4)	0-0.1	0.0-0.12
6/36	20(28.6)	19(27.1)	22(31.4)	25(35.7)	0.17-0.44	0.23-0.51
6/60	30(42.9)	30(42.9)	29(41.2)	25(35.7)	0.29-0.58	0.23-0.51
3/60	20(28.6)	20(28.6)	18(25.7)	18(25.7)	0.17-0.44	0.14-0.41
Total	70(100)	70(100)	70(100)	70(100)		

CI=Confidence interval by modified Wald Method.

patients less than that found in other studies.[15,16] Our study did not reveal any side effects after intravitreal bevacizumab consistent with the study of Minnella AM who also proved that it was effective in the regression of new vessels areas and the resolution of vitreous haemorrhages. This approach is potentially useful in allowing (within a planned temporal window) a safe and efficient panretinal photocoagulation to be performed while minimizing the risk of its complications.[15]

Another quasi-experimental study was conducted on 200 patients to assess the ocular complications after intra-vitreal Bevacizumab (Avastin) injection in eyes with choroidal and retinal neovascularization. Patients' average age in this study was 53.7 with (±SD =11.7) years. Majority of patients were given intravitreal bevacizumab due to diabetic retinopathy. Complications rate was only 24 (12%). Most prominent complication was sub conjunctival hemorrhage 12(50%) followed by Corneal Abrasion in 4 (16.7%). It was concluded that intravitreal Bevacizumab adverse effects were mostly procedure related.[17]

CONCLUSION

Intravitreal bevacizumab injection is effective in improving visual acuity in patients with proliferative diabetic retinopathy for short term results and this effect is more prominent with subjects having Diabetes Mellitus up to 10 years.

Limitations: Our study was single hospital based, with no focus upon status and reduction of diabetic macular edema, neovascularization, and clearing of vitreous hemorrhage before and after bevacizumab injection, as this injection has to be given for making patients suitable for laser photo coagulation therapy.

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Authors contribution:

MLAB designed the study, set objectives, did literature search and finalized the manuscript.
BK was involved in data collection, writing of the draft and literature search
KAM was involved in designing of study, critical review of the manuscript.
MUF helped in designing the study, data analysis and its interpretation, critical review and writing of final manuscript.