ORIGINAL ARTICLE

INTRAVITREL BEVACIZUMAB IN DIFFERENT TYPE OF RETINAL VEIN OCCLUSIONS

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Background: Retinal vein occlusion is frequent cause of visual loss with insufficient treatment options. Many treatment options have been tried in the past including intravitreal triamcenoloneacetonide injection. This study was conducted to evaluate the efficacy and complications of intravitreal injection of Bevacizumab in different types of retinal vein occlusion. **Methods:** This interventional study was carried out at Al Ibrahim eye hospital, Karachi from July 2011 to December 2012. Patients diagnosed with retinal vein occlusion of any type were included in the study using non-probability purposive sampling technique, after informed written consent. Patients were injected intra-vitreally with Bevacizumab 1.25 mg/0.05 ml under sterilized technique in operation room. Best corrected visual acuity and optical coherence tomography was repeated in every follow up along with the detailed fundoscopy and intraocular pressure measurement. Data analysis was done using SPSS-20.0. **Results:** A total 278 patients were included in the study according to the inclusion and exclusion criteria. Mean age of the patients was 54.28 years (SD=5.62). Out of 278 patients included in the study, 132 had BRVO, 141 had CRVO while 5 had HRVO. Mean visual acuity before injection was 2.309 lines of Snellen's acuity chart read, with minimum of 1 line read and maximum of 4 lines read (standard deviation=1.00). After 12 weeks post injection, 92 patients read 7 lines (6/6) of Snellen's visual acuity chart. Mean visual acuity was 4.75 lines of Snellen's acuity chart read, with minimum of 1 line read and maximum of 7 lines read (standard deviation=1.00). 77% of the patients had visual improvement after injection (p<0.05). **Conclusion:** Intravitreal bevacizumab injection is very effective in reducing macular thickness as well in improving visual acuity in all types of retinal vein occlusion.

Keywords: Visual improvement, macular thickness, bevacizumab, retinal vein, occlusion, intravitreal, outcome

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INTRODUCTION

Central retinal vein occlusion is one of most frequent vasuclar disorders in clinical practice. Green et al found venious thrombi in nearly all rubiotic eyes after CRVO, but it remains unclear whether venous thrombus formation reprents beginning or rather the endpoint of pathogenic cascade.[1]

Development of cystiod macular oedema (CME) is one of most common finding and also reason for decrease VA in CRVO. Impaired microcorculation and reduced blood flow leads to dysfunction of endothelial blood-retinal barrier with increased permibility and plasma exudation in to central retina.[2]

Retinal vein occlusion is the occlusion of either central retinal vein, branch retinal vein or in special circumstances hemi retinal vein occlusion. According to one study in which they combined the prevalence of 16 studies, the age- and sex-standardized prevalence of any RVO was 3.7 per 1000 in whites, 3.9 per 1000 in blacks, 5.7 per 1000 in Asians and 6.9 per 1000 in Hispanics. Similar study also reported that the prevalence for central retinal vein occlusion was lower than BRVO in all ethnic populations. This study estimated that 16.4 million adults are affected by Retinal vein occlusion. Out of which 2.5 million are affected by central retinal vein occlusion, while 13.9 million are affected by branch retinal vein occlusion.[3] One of the main cause of decreased vision after retinal vein occlusion is macular oedema. Many treatment options have been tried in the past including intravitreal triamcenoloneacetonide injection. Which has resulted in improvement of vision as well as resolution of macular oedema but at the expense of certain complications such as raised intra ocular pressure?[4] Bevacizumab is an off labelled drug in ophthalmology. Bevacizumab is an anti-vascular endothelial growth factor, thus it prevents capillary permeability and therefore results in decrease in macular oedema. Bevacizumab has been used successfully in many conditions such as age related macular degeneration, diabetic macular oedema, choroidal neovascularization and degenerative myopia. Many separate studies have been done on different types of retinal vein occlusions, such as central retinal vein occlusion[5] and branch retinal vein occlusion[6]. But not much data is available to compare its efficacy and complications between different types of retinal vein occlusions. Similarly, no such work has been done locally. Thus the aim of the study was to evaluate the efficacy and complications in different types of retinal

vein occlusions and compare its effectiveness among the different types. The rationale of the study is to identify a better alternative to other treatment options available that can result in better visual outcome and less complications.

MATERIAL AND METHODS

This is an interventional study, carried out at Al Ibrahim eye hospital, Karachi from July 2011 to December 2012. Ethical approval was taken from the ethical committee of Al-Ibrahim Eye hospital, Karachi.

Patients diagnosed with retinal vein occlusion of any type were included in the study using non-probability purposive sampling technique, after informed written consent. Patients having either cataract, corneal degeneration, bleeding disorders or raised intraocular pressure were excluded from the study. Patients included underwent detailed ophthalmic examination including examination using slit lamp bio-microscope and indirect ophthalmoscope. Intraocular pressure was taken using Goldman applanation tonometer. Macular thickness was measured using optical coherence tomography. Patients were injected intra-vitrealy with Bevacizumab 1.25 mg/0.05 ml under sterilized technique in operation room.

Best corrected visual acuity and optical coherence tomography was repeated in every follow up along with the detailed fundoscopy and intraocular pressure measurement. Data was entered on a pre-formed *pro forma*. Data analysis was done using SPSS version 20.0. Frequencies of age, gender and types of retinal vein occlusion was evaluated. Mean±SD was calculated for visual acuity and macular thickness. Paired *t*-test was used to compare the means between baseline and post treatment variables, while independent *t* test was used to compare the means between the different types of retinal vein occlusions.

RESULTS

278 patients were included in the study according to the inclusion and exclusion criteria. Mean age of the patients was 54.28 years (SD=5.62), with minimum age of the patient was 39 years while maximum age was 67 years. Out of these 278 patients 188 (67.6%) were male while 90 (32.4%) were females. In males the mean age was 54.90 years (standard deviation=5.75), while in females the mean age was 53.00 years (standard deviation=5.18) (Table-1).

Patients were divided in to 2 age groups of 26–40 years and greater than 40 years. Right eye was involved in 146 (52.5%) of the patients while 132 (47.5%) of the patients had left eye involvement. Thirty-six patients (12.9%) had diabetes mellitus while 146 patients (52.5%) had hypertension as co-morbid. Out of 278 patients included in the study, 132 had BRVO, 141 had CRVO while 5 had HRVO. Mean visual acuity before injection was 2.309 lines of Snellen acuity chart read, with minimum of 1 line read and maximum of 4 lines read (SD=1.00). Before injection the maximum any patient could have read was 4 lines (6/18) of Snellen's visual acuity, which was read by only 20 (7.2%) patients. While, on follow up 1 week after injection, 90 patients read 6 lines.

Mean visual acuity was 4.08 lines of Snellen acuity chart read, with minimum of 1 line read and maximum of 7 lines read (standard deviation=1.00). Similarly, improvement in the lines read was also noted in the follow up after 4 weeks post injection, over 68 patients read 6 lines or more of Snellen visual acuity chart. Mean visual acuity was 4.24 lines of Snellen acuity chart read, with minimum of 1 line read and maximum of 7 lines read (standard deviation=1.00).

After 12 weeks post injection, 92 patients read 7 lines (6/6) of Snellen visual acuity chart. Mean visual acuity was 4.75 lines of Snellen's acuity chart read, with minimum of 1 line read and maximum of 7 lines read (standard deviation=1.00). 77% of the patients had visual improvement after injection ($p<0.05$). Stratification was done with respect to age, gender and co-morbid and all were statistically non-significant ($p=0.591$, $p=0.36$ and $p=0.25$) respectively.

Mean Central macular thickness reduced from 478 microns to 287 microns ($p=0.031$).

Table-1: Change in visual acuity

	Baseline		After 1 week		After 4 weeks		After 12 weeks	
	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
7 lines read (6/6)	0	0	2	0.7	30	10.8	92	33.1
6 lines read (6/9)	0	0	90	32.4	68	24.5	72	25.9
5 lines read (6/12)	0	0	50	18.0	72	25.9	16	5.8
4 lines read (6/18)	20	7.2	12	4.3	20	7.2	10	3.6
3 lines read (6/24)	82	29.5	4	1.4	4	1.4	6	2.2
2 line read (6/36)	60	21.6	60	21.6	26	9.4	24	8.6
1 line read (6/60)	116	41.7	60	21.6	58	20.9	58	20.9
Total	278	100.0	278	100.0	278	100.0	278	100.0

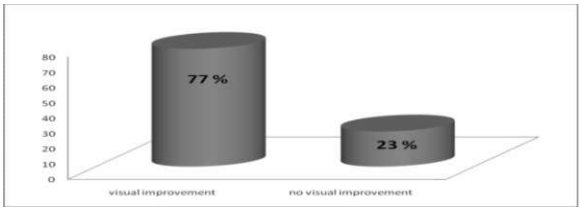

Figure-1: Visual outcome after injection

DISCUSSION

Many studies have shown successful results after intravitreal bevacizumab injection in patients with different types of retinal vein occlusions. One study on CRVO showed that the mean central macular thickness at baseline was 887 µm and decreased to a mean of 372 µm at month 1 (p<0.001). The mean baseline acuity was 20/600 (logMAR=1.48) and the mean acuity at month 1 was 20/200 (logMAR=1.05), a difference that was highly significant (p=0.001). At last follow-up, a mean of 3 months after the first injection, the mean visual acuity was 20/138 (logMAR=0.84), which was significantly better than baseline (p<0.001)[5] Another study on BRVO showed similar results as well. It showed The mean visual acuity improved from $20/200^{-}$ at baseline to $20/100^{-}$ at 1 month and $20/100^{+}$ at 3 months and last follow-up (p<0.001). The mean central 1 mm macular thickness was 478 µm at baseline and decreased to 310, 336, and 332 µm at 1 month, 3 months, and last follow-up (p<0.001).[7] In one study on CRVO and HRVO mean BCVA was 1.21 (Snellen equivalent, ≈20/320) in the affected eye before injection which improved to was 0.68 (Snellen equivalent, 20/100). Mean baseline CMT was 730.1 µm which reduced to 260.3 µm after the injection.[8] One retrospective study with 16 eyes found an improvement of VA in 87.5% of the eyes treated after three months.[9] Another retrospective study with 15 eyes an increase in VA of more than three lines in 40% of patients treated.[10]. In one prospective study, it was demonstrated that during OCT- guided per required need (PRN) treatment the mean time interval from previous injection before recurrence of macular oedema resulting from RVO ranged from 1.2 to 2.4 months.[11] Similarly our study also showed improvement in macular thickness as well as. The main limitations of our study were that it was conducted in a single centre and patients belong to single ethnic background as well.

CONCLUSION

Intravitreal bevacizumab injection is very effective in reducing macular thickness as well in improving visual acuity in all types of retinal vein occlusion.

AUTHOR'S CONTRIBUTION

DL, AUR: Conceived the idea, data collection, patient follow-up and write-up, UQ, AHT: Data analysis, literature search and final proof reading of the manuscript.

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