Original Article

Role of Bevacizumab (Avastin) in Diabetic Macular Edema

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ABSTRACT

Objective: To evaluate the efficacy of injection Bevacizumab (Intravitreal) in management of diabetic macular edema (DME).

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the completed at Ophthalmology department Nishtar Hospital Multan from March 2019 to March 2020.

Materials and Methods: Study was conducted on 60 eyes of 60 patients presented with diabetic macular edema. Intravitreal bevacizumab injection of 1.25 mg was administered 3.5 mm from the limbus under topical anesthetic drops. Follow up was done at 1st day and at 1 month duration after injection. Macular thickness was measured at every follow ups visit. SPSS version 23 was used for analysis of data. P value ≤ 0.05 was considered as significant.

Results: The mean pre Avastin macular thickness of the patients was 391.43±30.91 µm and after Avastin OCT at one month was 308.66±25.82 µm. Difference was found significant statistically, (p=0.000).

Conclusion: Diabetes leads to macular edema and retinopathy which is a hurdle in macular grid laser in such cases. Intravitreal injection of bevacizumab minimizes the exacerbation of macular edema in diabetic cases.

Key Words: Bevacizumab, Vascular Endothelial Growth Factor (VEGF), Macular thickness, Diabetic macular edema (DME).

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INTRODUCTION

Angiogenesis either physiological or pathological propagated by vascular endothelial growth factor which is a proangiogenic cytokine[1]. In condition of hypoxia vascular endothelial growth factor (VEGF) stimulate the endothelial cells which played an important role in pathophysiology of certain opthalmic diseases which may include neurovascular age related degenration, diabetic retinopathy, retinal vein occulusion[2,3]. This whole procedure results in loss of vision after hemorrhage, edema and retinal detachment after fibro vascular proliferation[4].

Anti VGEF therapy brings a revolution in treatment modalities of ocular disease[5]. First of all Pegaptanib was used and after that bevacizumab, Ranibizumab and Aflibercept were used successfully[6].

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Older therapeutic methods were photo dynamic therapy and neovascularization with laser photocoagulation, although these modalities were non physiologic and destructive in use[7]. In comparison to these methods, VEGF therapy is more potent and successful to inhibit the level of VEGF.

Now treatment of retinal diseases with anti VEGF is famous worldwide in clinical practice[8]. Number of injections increasing day by day in united states as in 2001 about 4215 injections were used in 2011 about 2.5 million injections. Similar ratio of increase in injections was noted in United Kingdom and Canada[9]. After anti VEGF therapy some local complications may occur like intraocular complications, ocular hemorrhage, rhegmatogenous retinal attachment and raised intraocular pressure[10].

MATERIALS AND METHODS

This prospective study was conducted at the department of Ophthalmology Nishtar Hospital Multan from March 2019 to March 2020. The hospital's ethics review board approved the all aspects of study. Patients who received anti VEGF therapy during the study period were included in the study. Informed written consents were obtained from patients before the start of procedure. Non probability consecutive sampling technique was used. Sample size was calculated by using an online software Openepi.com. Patients of the presumed or established endopthalmitis were enrolled in the study.

Patients with any degree of intraocular inflammation who required Intravitreal antibiotics were labeled as

presumed endopthalmitis. Positive gram stain and culture was used to approve the endopthalmitis. Patients in which endopthalmitis develops secondary to some other etiology or who did not fulfill the criteria of endopthalmitis were excluded from the study. All Intravitreal injections were performed in well designed operating rooms with standard protocols. A 29 gauge needle was used for administration in infra temporal quadrant. It was about 4mm distance from the limbus. Conjuctival anaesthesia was given with 4% lidocaine and 0.5% proparacaine. 5% povidone iodine solution was used to prepare eyelashes and eyelids. Patient's mouth and nose covered with surgical self adhesive drape. Sterile lid speculum was also used. Injections were administered by an ophthalmologist having 5 years experience in this procedure. Every patient was dealt after changing surgical sterile gloves and complete hand sepsis. Use of face masks and cessation of conversation at the time of injection administration was assured. A vitreous fluid of all patients sent to laboratory for microbial culture. Empiric treatment was started. Treatment modified according to the culture results.

SPSS version 23 was used for data analysis. Mean and standard deviation was calculated for categorical data. P value less than or equal to 0.05 was considered as significant.

RESULTS

Sixty patients were included, in this study. Intravitreal Injection of Bevacizumab was given to these sixty patients' sixty eyes. There were more males than females i.e. n=35 (58.3%) and n=25 (41.7%), respectively. The mean age of the patients was 52.91±3.25 years. The mean duration of diabetes of the patients was 12.61±4.15 years. n=11 (18.3%) eyes insulin dependent patients' and n=49 (81.7%) eyes were non-insulin dependent patients'. n=39 (65.0%) patients were controlled diabetes on medicine where as n=21 (35.0%) patients were found to be uncontrolled diabetes by medicine. (Table. I).

Table No.1: Baseline Characteristics of the Patients

Variable	Presence
Gender	
Male	n=35 (58.3%)
Female	n=25 (41.7%)
Age (years)	52.91±3.25
duration of diabetes (years)	12.61±4.15
Insulin dependent patient	n=11 (18.3%)
Insulin independent patient	n=49 (81.7%)
Controlled diabetes patient	n=39 (65.0%)
Un- controlled diabetes patient	n=21 (35.0%)

The mean pre Avastin macular thickness of the patients was 391.43±30.91 micrometers and post Avastin OCT after one month was 308.66±25.82 micrometers. The difference was statistically significant, (p=0.000). (Figure. I). It was seen that macular thickness after one month of injection was decreased in n=55 (91.7%) cases and increased in n=5 (8.3%) cases. Reduction in macular thickness was found as > 10% in n=46 (76.7%) cases, < 10% in n=9 (15.0%) cases and increased in n=5 (8.3%) cases. (Table. 2).

Table No.2: Reduction in Macular Thickness

Reduction in macular thickness	Presence
Yes > 10%	n=46 (76.7%)
Yes < 10%	n=9 (15.0%)
Increased	n=5 (8.3%)

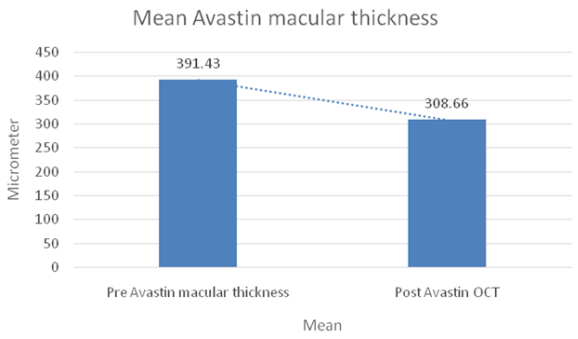

Figure No.1: Mean Avastin mascular thickness.

DISCUSSION

In patients of vitreous hemorrhage or media opacity it is difficult to perform laser therapy. Patients with neovascular glaucoma or iris neovascularization often present corneal edema or hyphema which is a hurdle in laser treatment[11]. Despite grid laser therapy in some cases macular thickness continue to increase in size. But in such cases Bevacizumab shows rapid and dramatic results and observed very effective that resolve complete macular edema in couple of days. Better outcomes associated with good diabetic control and compliance towards follow ups[12].

The mean age of the patients in our study was 52.91±3.25 years. A similar study was conducted by Mason et al[13] on 30 patients having mean age of 47.7 ± 12.5 years; another study was conducted by Avery et al[14] and observed mean age of 58 years which much higher than our study. Arevalo JF et al[15] reported a close enough observation of 53.2 years mean age in his study. Patients of these studies having diabetic retinopathy show variation in age limits may be due to geographical settings.

In our study mean duration of diabetes was 12.61±4.15 years. In a study by EI Haddad et al[16] reported that age of patient and duration of diabetes also associated with retinopathy but by logistic regression model lost the significance of diabetic duration which proves that it is not an independent risk factor. In a study by Ateeq A et al[17] reported mean duration of diabetes was 10.15 ± 3.2 years. This study also reveals that prevalence rate of

diabetic maculopathy is higher in cases with prolonged duration of diabetes.

In our study 18.3% eyes were insulin dependent and 81.7% eyes were non insulin dependent. In a study by Ateeq A et al[17] reported 18.5% were insulin dependent and 81.5% patients were noninsulin dependent. Regarding outcomes of study macular thickness after Bevacizumab a significant decrease in macular thickness (91.7%) was observed. Another similar study was conducted by Haritoglou et al[18] on diabetic macular edema treated with Bevacizumab 1.25mg and observed a significant decrease in macular edema (33%). Baseline macular thickness was 498.96±123.99 micrometers and after 1 month of injection thickness was 334.40±121.76 µm.

Another study was conducted by Ozkiriş et al[19] and concluded that Intravitreal administered of bevacizumab improves the thickness of macular edema and visual acuity, that why bevacizumab labeled as primary treatment of macular edema in diabetic cases. Joshi et al[20] observed in his study that hypertension and previous history of laser treatment are two main contributing predictor of Intravitreal injection of bevacizumab. But improvement in macular thickness reduction is observed.

CONCLUSION

Diabetes leads to macular edema and retinopathy which is a hurdle in macular grid laser in such cases. Intravitreal injection of bevacizumab minimizes the exacerbation of macular edema in diabetic cases.

Author's Contribution:

Concept & Design of Study:	Muhammad Awais Ashraf
Drafting:	Ghulam Abbas
Data Analysis:	Adeel Ahmed Siddiqui
Revisiting Critically:	Muhammad Awais Ashraf, Ghulam Abbas
Final Approval of version:	Muhammad Awais Ashraf

Conflict of Interest: The study has no conflict of interest to declare by any author.

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