

Mean Reduction In Foveal Thickness After Four Weeks Of Injection Bevacizumab (Avastin) Intravitreally For The Management Of Diabetic Macular Edema

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Abstract: Aim: To determine the mean reduction in foveal thickness after 4 weeks of Intravitreal Bevacizumab (Avastin) for the management of diabetic macular edema **Patients and methods:** This Quasi experimental study included 95 eyes of 95 patients, which were diagnosed with diabetic macular edema, and treated between November 2016 and May 2017 at Ophthalmology department of Jinnah Hospital, Lahore. The aim and procedure of study was explained and informed consent was taken from all patients. A detailed history and ocular examination in these cases was done. Basic ophthalmological examination was done. The macular thickness was assessed one week before procedure by OCT (Zeiss 4000). Injection Bevacizumab (avastin) 1.25mg/0.05 ml was given intravitreally under topical anesthesia 3.5-4mm away from limbus by researcher herself. After 4 weeks of injection, OCT was done on all patients and the outcome was decided on the modulation in thickness of of central maculi, which was recorded by the researcher herself. **Results:** The mean pre-procedure central macular thickness was 387.11+18.07µm which reduced to 318.75+18.87 µm at 4 weeks after treatment, the mean decrease was recorded as 68.36+7.60 µm; p value was 0.0001, showing a significant difference. **Conclusion:** The mean reduction in foveal thickness after 4 weeks of Intravitreal Bevacizumab (Avastin) for the management of diabetic macular edema is significantly different as compared with pre-treatment macular thickness. **Keywords:** Diabetic Macular Edema, Central Macular Thickness, Intravitreal Bevacizumab (Avastin), Mean Decrease.

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Introduction:

Diabetes mellitus (DM) is a common health problem in Pakistan. Our country is considered in top ten nations with higher frequency of Diabetes Mellitus in its population. In 2025, Pakistan may cross 10 million people having DM in its population.¹ Approximately 10% of the people aged >30 years are suffering from type II DM.² Patients with DM may have a serious eye diseases, without developing any symptoms, and this leads to the irreversible visual loss.³ The most common cause of impairment of vision in patients who are suffering from diabetes mellitus is macular edema. This edema

results from chronic increase of serum glucose levels. The persistent elevation of serum glucose leads to capillary damage which results in formation of micro aneurysms in the retina. These leaky micro aneurysms cause decrease in vision if leaky fluid involves foveal centre.⁴ Bevacizumab (Avastin, Genentech/Roche) is recombinant humanized monoclonal antibody, which is FDA approved for metastatic colorectal and breast cancer treatment. In under-developed and developing countries there is widely off label use of avastin by Ophthalmologists. The reason being, it is cost effective, easily available and has relatively good safety profile. In spite all having encouraging and good results in choroidal neovascularization, macular edema and diabetic retinopathy, there is no long-term guarantee on safety of Avastin.⁵ In a previous study, pre avastin mean foveal thickness was $384.38 \pm 40.51 \mu\text{m}$ and after one month of giving Avastin OCT showed mean thickness of $323.19 \pm 32.58 \mu\text{m}$, showing mean decrease as $61.19 \pm 7.93 \mu\text{m}$.⁶ Another study revealed that mean retinal thickness at baseline was calculated as $411 \pm 170 \mu\text{m}$ while after one month of Avastin it was recorded as $380 \pm 159 \mu\text{m}$, mean decrease was $31.0 \pm 11 \mu\text{m}$,⁷ i.e. $(0.031 \pm 0.011 \text{mm})$ which is significant difference from the previously mentioned study.

The rationale of the study is that the previous studies are showing significantly varying results, it needs another study to clarify the above variation in our targeted population and also record the mean decrease of central macular thickness in our population, the results of the study would also be helpful for timely

management of the morbidity.

Patients and methods:

This Quasi experimental study included 95 eyes of 95 patients, which were diagnosed with diabetic macular edema, and treated between November 2016 and May 2017 at Ophthalmology department of , Jinnah Hospital, Lahore.

The aim and procedure of study was explained and informed consent was taken from all patients. A detailed history and ocular examination in these cases was done. Basic ophthalmological examination was done. The macular thickness was assessed one week before procedure by OCT (Zeiss 4000). Injection Bevacizumab (avastin) $1.25 \text{mg}/0.05 \text{ml}$ was given intravitreally under topical anesthesia $3.5\text{-}4 \text{mm}$ away from limbus by researcher herself. After 4 weeks of injection, OCT was done on all patients and the out come was decided on the modulation in thickness of of central maculi, which was recorded by the researcher herself.

The data was recorded in a pre-designed performa analyzed using Statistical Package for Social Sciences (SPSS, IBM Statistics, Chicago, IL, USA version 23.0) standard and Mean deviation was calculated for quantitative variable like age, pretreatment macular thickness, post treatment macular thickness and mean decrease in thickness in fovea after 4 weeks of Intravitreal Bevacizumab (Avastin) was recorded. Frequencies and percentages were calculated for qualitative variables like sex of the patients. Paired sample t test was used to compare before and after treatment macular thickness. if p value < 0.05 was considered as significant. Stratification for age, gender and duration of disease was recorded to address the

effect modifiers. Post stratification paired t test was applied to see the significance. P value <0.05 was considered as significant.

Results:

The study included 95 eyes to determine the mean reduction in thickness of fovea after 4 weeks of Injection Bevacizumab (Avastin) intravitreally for the management of diabetic macular edema. Age distribution of the patients showed that 45.26%(n=43) were between 40-55 years of age whereas 54.74%(n=52) were between 56-70 years of age, mean \pm SD was calculated as 55.63+8.40 years. (Table No. 1) Gender distribution of the patient showed that 61.05%(n=58) were male whereas 38.95%(n=37) were females. (Table No. 2) The mean pre-treatment central macular thickness was 387.11+18.07 μ m which reduced to 318.75+18.87 μ m at 4 weeks of injection Bevacizumab (Avastin) intravitreally; mean decrease was recorded as 68.36+7.60 μ m, p value was 0.0001, showing a significant difference. (Table No. 3) Stratification for age, gender and duration of disease was recorded to approach the modifying agents. Post stratification paired t test was applied to see the significance but we recorded no significant difference regarding these characteristics. (Table No. 4-6)

Discussion:

The quite frequent cause of impairment of vision in patients who are suffering from diabetes is diabetic macular edema. This macular edema affects 75000 new patients per annum in United States. The leading cause of loss of vision in patients who are

suffering from diabetes is diabetic retinopathy and macular edema which affects working age adults. To regain vision in patients of macular edema, the researchers are very interested and trying to find other treatment modalities for diabetic macular edema⁸ Several studies have shown the increasing effectiveness of anti- VEGF agents when compared to macular laser photocoagulation and now they are accepted as first line agents to treat Diabetic macular edema, particularly involving the centre of fovea⁹⁻¹³ In under-developed and developing countries there is widely off label use of avastin by ophthalmologists. The reason being, it is cost effective, easily available and has relatively good safety profile.^{14,15} In spite all having encouraging and good results in choroidal neovascularization, macular edema and diabetic retinopathy, there is no long-term guarantee on safety of Avastin. Arevalo JF et al demonstrated in their study that Bevacizumab has a similar efficacy profile, when compared to Aflibercept and Ranibizumab in treatment of diabetic foveal thickness having mild to moderate loss in vision.¹⁶ Ross et al demonstrated the cost effectiveness of Bevacizumab in the treatment of diabetic macular edema, as compared to aflibercept and ranibizumab, with modest differences in efficacy.¹⁷ This study was conducted with the view that the previous studies were showing significant variant results, it needs another study to clarify the variation and also record the mean decrease of central macular thickness in our population, the results of the study would also be helpful for timely management of the morbidity. In this study, out of 95 cases, 45.26%(n=43) were between 40-55 years of age whereas

54.74%(n=52) were between 56-70 years of age, mean+SD was calculated as

55.63+8.40 years,

Age(in years)	No. of patients	%
40-55	43	45.26
56-70	52	54.74
Total	95	100
Mean±SD	55.63±8.40	

Gender	No. of patients	%
Male	58	61.05
Female	37	38.95
Total	95	100

Macular thickness (µm)	Mean	SD	P value
Pretreatment	387.11	18.07	
Post treatment	318.75	18.87	0.0001
Mean decrease	68.36	7.60	

Age(in years)	Mean	SD	P value
40-55	68.37	8.07	0.986
56-70	68.35	7.26	

Gender	Mean	SD	P value
Male	68.50	7.82	0.82
Female	68.14	7.34	

Duration	Mean	SD	P value
1-5 years	68.52	7.70	0.77
>5 years	68.03	7.51	

61.05%(n=58) were male whereas

38.95%(n=37) were females. At 4 weeks

of Injection Bevacizumab (Avastin) intravitreally for the management of diabetic macular edema, the mean reduction in thickness of fovea was recorded, it was $387.11 \pm 18.07 \mu\text{m}$ before treatment and reduced to $318.75 \pm 18.87 \mu\text{m}$ after treatment, the mean decrease was recorded as $68.36 \pm 7.60 \mu\text{m}$, p value was 0.0001, showing a significant difference. We compared our results with a previous study, showing that mean macular thickness before injection of Avastin was 384.38 ± 40.51 micrometers and after one month post injection OCT showed mean thickness of 323.19 ± 32.58 micrometers showing mean decrease as $61.19 \pm 7.93 \mu\text{m}$.⁶ Another study revealed that mean retinal thickness at baseline was calculated as $411 \pm 170 \mu\text{m}$ while after one month of Avastin it was recorded as $380 \pm 159 \mu\text{m}$, mean decrease was $31.0 \pm 11 \mu\text{m}$,⁷ i.e. ($0.031 \pm 0.011 \text{mm}$) which is significantly different. It also shows a significant difference from the previous mentioned study. Seo JW and Park done a study which showed that injection Bevacizumab intravitreally has resulted a significant improvement after one week of injection in central macular thickness as well as in best corrected visual acuity (BCVA) this advantageous and good effect continued for up to 3 months. Despite that the little reduction in this improvement at months suggests that this is necessary to repeat bevacizumab injection after three months.¹⁸ Soheilian et al¹⁹ reported significant foveal thickness reduction in patients eyes who were injected Avastin and Avastin/triamcinolone only up to 6 weeks after treatment.

There is another series of 11 patients who underwent vitrectomy previously did not Journal of Peoples University of Medical & Health Sciences for women Nawabshah SBA. 2020; 10(1)

showed any progress in vision or foveal thickness after treatment with intravitreal bevacizumab. This insufficient improvement in best corrected visual acuity and foveal edema could be due to persistent photoreceptor damage from extended period of disease or from previous extensive treatment.²⁰

There are some limitations of this study which include short duration, non randomized and uncontrolled which hinders any estimation of the long term efficacy or safety of Bevacizumab injection intravitreally. In addition to this, in our study there was no control group, so we can not eliminate the possibility that some of reduction in macular edema might be associated good systemic health and good control of sugar level. When patients are involved in a clinical trial or new treatment, it is not uncommon that supplementary attention is directed towards promoting systemic health.

Conclusion:

The results reveal that mean reduction in foveal thickness after 4 weeks of Injecting Bevacizumab (Avastin) intravitreally for the management of diabetic macular edema is significantly different when compared with pre-treatment macular thickness. In addition, keeping in view, the general economic status of patients in our local population, Intravitreal Bevacizumab (Avastin) is cost effective and has good Efficacy-profile.

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