Research Article

# Prophylactic Role of Intra-Vitreal Bevacizumab(Avastin) in Diabetic Patients Under Going Phacoemulcification

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## Abstract

**Objectives:** To study the effect of pre-operative intra-vitreal Avastin (bevacizumab) in diabetic patients undergoing phacoemulcification on central macular thickness and best corrected visual acuity.

**Methods:** A randomized controlled trial was conducted which included 42 patients (N=42). Group A and B had 21 patients each. Group A patients received injection Avastin (Bevacizumab) one week before phacoemulcification and Group B patient underwent phacoemulcification alone. Pre-operative best corrected visual acuity (BCVA) and central macular thickness (CMT) was recorded before giving intra-vitreal bevacizumab. Post-operative BCVA and CMT was noted 4 weeks after the surgery.

**Results:** The difference in final visual acuity between Group A and B was not statistically significant. Change in CMT from pre-operative value was not significant in study population (p=0.364), but was statistically significant in both groups individually (p=0.029, 0.001 respectively).

**Conclusion:** Our study concludes that cataract surgery along with prophylacticintra-vitreal Avastin (bevacizumab) may contribute in short term improvement of macular thickness, but does not have any statistical significant effect on final BCVA.

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**Keywords** | Bevacizumab (Avastin), Phacoemulcification, Best Corrected Visual Acuity, Centeral Macular Thickness (CMT)

## Introduction

Diabetes is highly prevalent disease. The number of diabetics is on the rise and has almost doubled in the past two decades.[1] The prevalence of any diabetic retinopathy and sight-threatening diabetic retino-pathy in those with type 1 diabetes was 56.0% and 11.2%, respectively, and in type 2 diabetes was 30.3% and 2.9%, respectively.[2] According to World Health Organization (WHO), prevalence of Diabetes in Pakistan is 10 %, which is almost 12.9 million individuals.

`Vascular endothelial growth factor (VEGF) can disturb blood retinal barrier significantly. It effects endothelial tight junction proteins which increases retinal permeability resulting in retinal edema[3]. This sequence of events forms the very basis of diabetic retinopathy pathogenesis.

Cataract is defined as development of opacities in crystalline lens. Framingham, Massachusetts study showed that 15 % of study population between age group of 52-85 years had reduced visual acuity due to cataract. Around 1 million cataract surgeries are performed in United States each year and almost 5 to

10 million individuals suffers from visual disability due to cataract.

Phacoemulsification when performed in diabetic patients, has shown to increase the progression of diabetic retinopathy and diabetic maculopathy.[4] A lot of factors play their role in worsening of diabetic retinopathy after cataract surgery. It includes duration of diabetes, diabetic control, condition of retina at the time of surgery, duration of surgery and per-op complications. Mostly, retinal changes are reversible and improve with time and medication. At times conditions like diabetic macular edema doesn't resolve even with medication and there is a permanent decrease in the visual acuity.

Bevacizumab ( Avastin) is a humanized therapeutic form of anti-VEGF antibody, blocking angiogenesis.[5] It inhibits all active isoforms of VEGF. Previously it has been used in tumor therapy. This anti-angiogenesis effect of bevacizumab can be used in the treatment of diabetic retinopathy to counter the effect of vascular endothelial growth factor. Intravitreal bevacizumab has shown marked regression of retinal neovascularization in patients with proliferative diabetic retinopathy.[6,7,8] Macular edema, in association with wet age related macular degeneration (AMD) and central retinal vein occlusion(CRVO) can also be treated with intra-vitreal Bevacizumab.

Recent studies have shown that in diabetic population, anti-VEGF given along with phacoemulcification reduces the chances of worsening of diabetic retinopathy and maculopathy.[9] Preoperative intravitreal anti-VEGF is not a standard protocol in Pakistan, or anywhere else in the world. We expect different results in our local population because, due to lack of resources and awareness, diabetes is poorly controlled in our population, as compared to the rest of the world. Because of this, the severity of diabetic retinopathy in developing countries like Pakistan is also different and its response to cataract surgery alone or with preoperative intravitreal Avastin (bevacizumab) is also expected to be different.[10] If my study shows that the preoperative injection of Avastin (bevacizumab) does in fact helps in slowing down the progression of diabetic retinopathy in patients undergoing cataract surgery, it will advocate putting this practice in the standard protocol for diabetic patients undergoing cataract surgery.

## Methods

Study was conducted in the Eye department, Mayo hospital, Lahore. Permission was taken from ethical review board. Total 42(N=42) patients having cataract included in the study, were randomly assorted in to group A and B. Group A included 21 patients, out of which 9(42.8%) were females. Age ranged from 45 -70 years, with an average of 54.09 years. Duration of diabetes was between 7-12 years with an average of 9.76 years. Group B included 21 patients (10 were females). Age ranged from 40-70 years with an average of 56.8 yrs. Duration of diabetes was between 7-12 years with an average of 9.45 years. All patients in group A and B were having moderate to severe NPDR without macular edema. There was no previous history of ocular surgery, intra-vitreal injection, trauma or sub-tenon injection. Best corrected visual acuity (BCVA) in group A patients was between 0.1 to 0.33 log MAR with an average of 0.19 log MAR. Central macular thickness (CMT) taken one week before surgery ranged from 180-250 microns with an average of 210.5 microns. BCVA in group B was between 0.1-0.3 Log MAR with an average of 0.19 log MAR. CMT was recorded between 180-230 microns with an average of 204.5 microns. Both groups had base line investigations done before surgery. Patients with uncontrolled blood pressure, diabetes and blood cholesterol levels were referred to internist to control their blood pressure. All surgeries were done by single surgeon.

Patients in group A, received intra-vitreal Bevacizumab one week before cataract surgery. All the patients were given topical antibiotics after injection and called after one week when phacoemulcification was performed. Any patient who had any per-op complication like vitreous loss was excluded from the study. After phacoemulcification, non-foldable 5.5 mm lens was implanted and a stitch was applied on the limbus wound. Topical antibiotics and steroids were advised to all the patients. Follow up was done at 1$^{st}$ day, 7$^{th}$ day and 4$^{th}$ week. BCVA and CMT was recorded on 4$^{th}$ week.

Patients in group B, underwent phacoemulcification with same protocols as in group A. All patients were given similar post-operative topical treatment as group A. follow up was done on 1$^{st}$ day, 7$^{th}$ day and 4$^{th}$ week. BCVA and CMT were recorded at 4$^{th}$ week.

Data were statistically analyzed through statistical program for social sciences (SPSS) version 17. Age, CMT, duration of diabetes , BCVA were described in terms of mean and standard deviation. Gender and laterality were documented in terms of frequency and percentage. To check data normality, Shapiro Wilk's test was applied. For comparison between change in pre and post-operative central macular thickness and best corrected visual acuity, paired t test was used.The change in BCVA and CMT between groups was checked using independent t test. P value was considered significant when it was less than 0.05.

## Results

Our study included 42 eyes (42 patients). Table 1 shows clinical and demographic data of our study population. There was no difference between groups in terms of age, gender, laterality and duration of diabetes. (p= 0.303, 1, 0.758, 0.458 respectively).

**Table 1** *Demography and Clinical Data of Study Population (n=42)*

| Variable | Study Population (n=42) | Group A (n=21) | Group B (n=21) | p Value* (between groups) |
|---|---|---|---|---|
| Age (Years) Mean ± SD | 55.48±8.58 | 54.09±9.25 | 56.86±7.84 | 0.303 |
| Gender (Male/Female) | 20/22 (47.6%)/ (52.4%) | 10/11 (47.6%)/ (52.4%) | 10/11 (47.6%)/ (52.4%) | 1 |
| Laterality Right/Left | 21/21 (50%)/(50%) | 11/ 10 (52.4%)/(47.6%) | 10/ 11 (47.6%)/ (52.4%) | 0.758 |
| Duration of diabetes (Years) Mean ± SD | 9.59±1.43 | 9.76±1.41 | 9.43±1.47 | 0.458 |

* Paired t test for quantitative variables, Chi square test for qualitative variables

**Table 2:** *Change in BCVA and CMT in Study Population and Grups (n=42)*

| Variable | Study Population (n=42) | Group A (n=21) | Group B (n=21) | p Value* (between groups) |
|---|---|---|---|---|
| Pre-Operative BCVA (logMAR) Mean ± SD | 0.21±0.81 | 0.24±0.75 | 0.19±0.08 | 0.058 |
| Post-Operative BCVA (logMAR) Mean ± SD | 0.58±0.13 | 0.59±0.13 | 0.57±0.13 | 0.571 |
| Pre-Operative CMT (µm) Mean ± SD | 208.09±17.60 | 210.95±19.01 | 205.24±16.01 | 0.298 |
| Post-Operative CMT (µm) Mean ± SD | 211.67±34.07 | 200.01±30.82 | 223.33±33.81 | 0.025 |

*Independent t Test

**Table 3:** *Change in BCVA and CMT within Groups (n=42)*

| Variable | Study Population (n=42) | Group A (n=21) | Group B (n=21) |
|---|---|---|---|
| Pre-Operative BCVA (logMAR) Mean ± SD | 0.21±0.81 | 0.24±0.75 | 0.19±0.08 |
| Post-Operative BCVA (logMAR) Mean ± SD | 0.58±0.13 | 0.59±0.13 | 0.57±0.13 |
| p Value (BCVA)* (within group) | <0.001 | <0.001 | <0.001 |
| Pre-Operative CMT (µm) Mean ± SD | 208.09±17.60 | 210.95±19.01 | 205.24±16.01 |
| Post-Operative CMT (µm) Mean ± SD | 211.67±34.07 | 200.01±30.82 | 223.33±33.81 |
| p Value (CMT)* (within group) | 0.364 | 0.029 | 0.001 |

*Paired t Test

Table 2 shows mean pre and post-operative central macular thickness and best corrected visual acuity. Our analysis showed that the difference in pre-operative centeral macular thickness, pre and post-operative visual Acuity (BCVA) between two groups was statistically insignificant (p=0.298,0.058, 0.571 respectively). Difference in mean change in CMT between groups was statistically significant (p= 0.025). Mean change in BCVA and CMT in study population and within each group is given in Table 3. Change in BCVA from pre-operative value was statistically significant in study population, group A and group B (p<0.001). Change in CMT from pre-operative value was not significant in study population (p=0.364), but was statistically significant in both groups individually (p=0.029, 0.001 respectively). This was observed because CMT significantly increased from baseline pre-operative value in Group B, while it was significantly reduced from pre-operative value in Group A.

## Discussion

In modern world, cataract surgery is considered to be a type of refractive procedure with very high expectations. Surgical outcomes not only depend upon the good surgical technique, number of other factors interplay for final results. In presence of diabetes, cataract surgery becomes comparatively difficult and ophthalmologist has to keep in mind number of important variables for a good surgical outcome.

Our study was based on the observation that diabetic patients are prone to progression of retinopathy when a surgical trauma like phacoemulcification is performed.[11] This progression was documented in 20 % of Diabetic patients within 12 months of phacoemulcification .[12]

We performed a randomized case control trial in order to study our observation. Two groups of randomly assorted patients underwent phacoemulcification with and without injection of intra-vitreal bevacizumab (IVB). Pre and post operative BCVA and CMT at 4 weeks were compared.

Our study showed that both groups had significant improvement in final visual acuity. Group A (phaco withIVB) had mean BCVA of 0.59 +/- 0.13 Log MAR and Group B (Phaco only) BCVA was 0.57 +/- 0.13 Log MAR. Study population mean BCVA was 0.58+/- 0.13Log MAR. There was no statistically significant difference in final BCVA of both groups. A meta-analysis results showed that corrected distance vision acuity measured at 1 month and 3 months after cataract surgery was significantly better in the IVB groups than in the control groups ($P < 0.00001$ and $P = 0.01$), whereas the corrected distance vision acuity at 6 months did not vary significantly between the 2 groups ($P = 0.24$).[13] A prospective randomized study conducted by Fard MA[14] to study the prophylactic use of intra-vitreal bevacizumab for diabetic macular edema after cataract surgery showed no difference in final visual acuity in two groups. However another study conducted by Takamura Y on diabetic patients with diabetic maculopathy under going phacoemulcification[15], showed a significant difference in improvement of post-op BCVA in patients underwent cataract surgery with IVB.

## Conclusion

Our study concludes that cataract surgery along with prophylactic intra-vitreal bevacizumab may contribute in short term improvement of macular thickness, but does not have any statistical significant effect on final BCVA.

**Ethical Approval: Given**
**Conflict of Interest: None**
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