Original Article

Intra-Operative Intravitreal Bevacizumab for Patients with Diabetic Macular Edema Undergoing Phacoemulsification with Foldable Intraocular Lens (IOL) Implantation

Haider Ali Chaudhry, Gulnaz, Irfan Ahmed Sualeh, Muhammad Ahmad

ABSTRACT:

Objective: To assess the efficacy of Intra-operative Intravitreal Bevacizumab in treating Diabetic Macular Edema in patients undergoing Phacoemulsification with Foldable intraocular lens (IOL) Implantation, in comparison to a control group.

Methodology: This experimental study was performed in department of Ophthalmology, Madinah Teaching Hospital, Faisalabad from 5th October to 2022 – 5th March 2023. Sixty patients (30 in each group) were enrolled in the study. Patients in group "A" received Intravitreal Bevacizumab immediately after phacoemulsification with foldable IOL implantation. Whereas Intravitreal Bevacizumab was not given to patients in group B (control group). Best Corrected Visual Acuity (BCVA) and macular thickness using optical coherence tomography (OCT) were recorded within a timeframe of 7-30 days prior to surgery, as well as at 1 and 3 months after the surgery for comparison between the two study groups. Data analysis conducted using SPSS version 23. $P \leq 0.05$ considered significant.

Results: The study comprised 60 patients, with a mean age of 56.43 ± 5.90 years, representing both genders. Among the participants, males were predominant, accounting for 32 (53.3%) individuals, while females constituted 28 (46.7%) of the sample. The baseline best-corrected visual acuity (BCVA) measurements between group A and group B were 0.22 ± 0.68 and 0.21 ± 0.07, respectively. There was no statistically significant difference observed between the two groups (P = 0.677). However, significant disparities in BCVA were observed after one- and three-months post-surgery, favoring group A. Similarly, mean optical coherence tomography (OCT) at baseline was 271.09 ± 26.87 in group A and 307.57 ± 32.81 in group B, with no significant difference (P = 0.771). Nonetheless, significant differences in OCT were noted after one- and three-months post-surgery, with group A demonstrating superior results. These findings underscore the beneficial impact of intra-operative Bevacizumab in improving both BCVA and OCT outcomes post-surgery.

Conclusion: The administration of intravitreal bevacizumab during phacoemulsification has been shown to yield notable improvements in Best Corrected Visual Acuity (BVCA) and Optical Coherence Tomography (OCT) among those with diabetes with macular edema who are undergoing cataract surgery.

KEYWORDS: Best-corrected visual acuity, Optical Coherence Tomography, Macular edema, Intravitreal Bevacizumab, Phacoemulsification Surgery, Diabetic Retinopathy.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by elevated levels of glucose in the bloodstream resulting from from impaired insulin production and responsiveness.[1] Diabetes is characterized by frequent urination and excessive thirst. If left untreated, it can lead to a slew of consequences.[2] In diabetic individuals, chronic hyperglycemia and other metabolic abnormalities contribute to the deterioration of this barrier. Consequently, an elevated permeability of blood vessels inside the retina occurs, resulting in the release of fluid and proteins into the adjacent retinal tissue. Macular edema is a prevalent consequence of diabetic retinopathy and can have a substantial impact on visual function.[3,4] Retinal thickness or the presence of hard exudates surrounding one disk diameter of

Haider Ali Chaudhry,[1] *MBBS, FCPS*
Senior registrar
Gulnaz,[2] *MBBS, FCPS*
Consultant
Irfan Ahmed Sualeh,[3] *MBBS, FCPS, FRCS*
PGR Vitreoretinal Ophthalmology
Muhammad Ahmad,[4] *MBBS*
PGR Ophthalmology
[1,3-4]Madinah Teaching Hospital, FSD, PAK.
[2]Primary & Secondary Health Department, FSD, PAK.

Correspondence:
Haider Ali Chaudhry,
haiderali.choudhry@gmail.com

the macula's center is a common characterization. Macular edema is the predominant etiology of visual impairment among patients with diabetes, affecting approximately 14% of this population. Extended hyperglycemia disturbs the Blood retinal barrier (BRB), leading to the buildup of fluid and macromolecules. This leads to an increase in Vascular endothelial growth factor (VEGF) expression because of oxidative damage.[4]

The clinical management of retinal diseases primarily encompasses a range of treatment modalities including laser photocoagulation, alongside pharmacological therapies such as bevacizumab, ranibizumab, and triamcinolone acetonide. Additionally, targeted combination therapies are also being increasingly explored as part of comprehensive treatment approaches. By combining surgical and pharmacological interventions tailored to the specific needs of individual patients, clinicians can optimize outcomes and improve the overall management of retinal illnesses.[5,6]

Phacoemulsification is one the most popular surgical treatments done on diabetes patients worldwide.[7] Given the importance of VEGF in the evolution of diabetic macular edema (DME), the development of anti-VEGF medicines for the prevention and treatment of post-cataract surgery diabetic macular edema (DME) has piqued the interest of researchers. Bevacizumab is a widely used off-label treatment for DME that inhibits all VEGF isoforms.[7] Multiple studies have reached the consensus that the administration of intravitreal bevacizumab during phacoemulsification yields enhancements in best corrected visual acuity (BCVA) and reductions in macular thickness among persons with preexisting macular edema.[7,8]

We aimed to assess the efficacy of Intra-operative Intravitreal Bevacizumab in treating Diabetic Macular Edema in patients undergoing Phacoemulsification with Foldable intraocular lens (IOL) Implantation, in comparison to a control group. This study not only serves as a scientific investigation but also makes a valuable contribution to the continuously developing field of medical science by meticulously and accurately deciphering the complexities of ocular health.

METHODOLOGY

This experimental study was conducted in the Ophthalmology Department at Madinah Teaching Hospital (MTH) in Faisalabad during 5th October to 2022 – 5th March 2023 after taking ethical approval with #MTH/FSD/Ophth /0127. The sample size was determined at 5% significance level, 95% CI and proportion using the WHO sample size calculator, amounted to 60 participants. Inclusive criteria embraced individuals aged over 18, presenting with clinically significant macular edema who were enrolled by purposive sampling technique in this study, while exclusions were comprehensive, patient with proliferative diabetic retinopathy, massive vitreous hemorrhage, traction membranes, additional retinal conditions, or a history of ocular trauma or surgery were excluding from the study.

The patients were randomly assigned to either Group-A, which received single dose of Intravitreal Bevacizumab 1.25mg / 0.05ml intraoperative immediately after phacoemulsification with foldable IOL implantation, or Group-B (control group, which did not receive Intravitreal Bevacizumab along with phacoemulsification. Ethical considerations were paramount, with participants from the eye OPD gaining entry post clearance from the hospital's ethical committee. The informed consent process was conducted meticulously to ensure voluntary and informed participation.

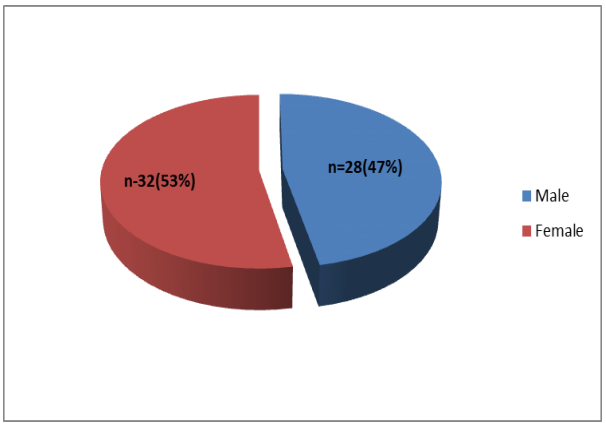
The study's foundational component involved conducting ophthalmologic examinations, which involved the evaluation of parameters such as Best Corrected Visual Acuity (BCVA) and macular thickness using optical coherence tomography (OCT). The diagnostic repertory was enhanced by the inclusion of fundus images and fluorescein angiography. The baseline characteristics were obtained by measuring BCVA using the Snellen

test. BCVA and OCT measurements were documented within a timeframe of 7-30 days prior to surgery, as well as at 1 and 3 months after the surgery as primary outcomes. A significance level of $P \leq 0.05$ was maintained for the data analysis conducted using SPSS version 23.

RESULTS

The study involved 60 patients with a mean age of 56.43 years, with a standard deviation of 5.90 years. The participants included both males and females. Among the study sample, there were 32 male patients, accounting for 53.3% of the total, while females comprised 28 patients, constituting 47% of the total, as indicated in figure 1.

Figure 1: Gender Distribution of the Patients (n=170)



The Best Corrected Visual Acuity (BCVA) values at the beginning of the study were 0.22 ± 0.68 in group A and 0.21 ± 0.07 in group B. There was no statistically significant difference found between the two groups (P = 0.677), as shown in Table 1. However, a significant disparity in BCVA was detected in both groups after one- and three-months post-surgery, with group A demonstrating superior BCVA in comparison to group B.

Table-1: - Best Corrected Visual Acuity before and After Cataract Surgery in study groups (n=60)

Visual Acuity	Group		P Value
	A	B	
Before surgery	0.22 ± 0.68	0.21± 0.07	0.677
After one 1 months	0.33± 0.31	0.26 ±0.10	0.000*
After 3 months	0.42±0.12	0.31 ± 0.24	0.004*

Level of significance set at p value ≤ 0.05

At baseline, the mean macular thickness obtained by Optical Coherence Tomography (OCT) measurement was 271.09 ± 26.87 in group A and 307.57 ± 32.81 in group B, with no significant difference observed between the two groups (P = 0.771), as presented in Table 1. However, after one- and three-months post-surgery, a significant difference in OCT measurements was noted in both groups, with group A demonstrating better OCT results compared to group B.

Table-2: Optical Coherence Tomography before and After Cataract Surgery in Study groups (n=60)

Optical Coherence Tomography (OCT)	Group A	Group B	P value
	Macular Thickness Mean ± SD	Macular Thickness Mean ± SD	
Before surgery	271.09 ± 26.87	307.57± 32.81	0.771*
After one 1 months	266 ± 0.02	326 .86±31.02	0.000*
After 3 months	236.40 ±26.39	351. 53 ±27.63	0.002*

Level of significance set at p value ≤ 0.05

Discussion

Individuals with diabetes exhibit an increased vulnerability to the development of cataracts in comparison to those without diabetes. Approximately 20% of cataract procedures in the Western world are performed on individuals with diabetes, according to estimates. Diabetic macular edema (DME) is the predominant factor contributing to inferior visual results in diabetic patients following cataract surgery.[9] The etiology of DME following cataract surgery remains uncertain; never-the less, it is plausibly associated with an imbalance in growth factors, cytokines, and inhibitory factors. Angiogenesis and vascular permeability are regulated by these variables, potentially leading to alterations in the inner blood-retinal barrier and an elevation in macular edema.[10] A number of studies have recommended intravitreal steroids or bevacizumab for patients with DME having phacoemulsification in order to enhance the final morphological outcome of therapy. The current study included 60 patients of both genders with a mean age of 56.43 ± 5.90 years. The number of male patients in the research sample was 32

(53.3%), while females were 28 (46.7%). The findings are consistent with previous research.[11,12]

Group A had a baseline BCVA of 0.22 ± 0.68, while group B had a baseline BCVA of 0.21 ± 0.07. There was no significant difference between the two groups (P 0.677). At one and three months following surgery, a notable disparity in BCVA was observed between the two groups, with group A exhibiting superior BCVA. The average central macular thickness (CMT) at the beginning of the study was 271.09 ± 26.87 in group A and 307.57 ± 32.81 in group B. There was no significant difference between the two groups (P 0.771). A notable disparity in OCT was observed between the two groups after one and three months of surgery. The research findings indicate that the average initial BCVA was 0.100.04, with a range of 0.05-0.2. The average BCVA values were 0.47 ± 0.16 (0.2-0.5) and 0.51 ± 0.12 (0.3-0.6) a month and three months after the procedure, respectively. The BCVA levels measured at one and three months post-surgery were significantly higher than the initial BCVA of the patient (P = 0.004).[13]

According to our data, the administration of intra-operative injection of IVB resulted in a decrease in central macular thickness (CMT), but no administration of the injection during cataract surgery led to an increase in CMT. In addition, it was shown that the CMT increased to over 300µm in eyes treated with phacoemulsification only compared to those treated with the combination operation. The initial average CMT prior to the two procedures did not exhibit significant differences. However, subsequent to the administration of the injections, the results were reversed. Hence, the utilization of intra-operative IVB injection resulted in a more efficient reduction of CMT compared to the control group. Addition-ally, we conducted an investigation of the proportion of eyes exhibiting heightened sensitivity.[14]

Previous Pakistani study in the same field is in agreement with current results and reported early improvement in BCVA after intravitreal injection of Bevacizumab (IVB)for DME at follow-ups of 1 and 3 months than control group on laser photocoagulation.[15] Previous research has demonstrated that patients with coexisting DME have poor visual outcomes following cataract surgery; in a previous research only 53% achieved a postoperative BCVA 6/12, and that over half of them had either no discernible improvement in vision or, worse, had lost all vision.[16] This stands in sharp contrast to the visual outcomes observed in patients without diabetes following cataract surgery, when over 95% obtain a BCVA of 6/12 or better.[17] Study was done on small population evaluated was limited, and the follow-up period was short, despite the fact that our study is interesting and shows the value of bevacizumab in surgery.

In diabetic patients with macular edema who are undergoing cataract surgery, the utilization of intravitreal bevacizumab as an intra-operative intervention during phacoemulsification has been shown to yield more favorable results in terms of best-corrected visual acuity (BCVA) and central macular thickness (CMT). Clinicians have the ability to improve visual outcomes and reduce the negative effects of diabetic macular edema on postoperative recovery by injecting bevacizumab during cataract surgery. The results indicate that including intra-operative intravitreal bevacizumab in the treatment plan for diabetic patients who are undergoing cataract surgery shows significant potential for improving visual results and increasing overall patient contentment.

Findings of current study contribute valuable insights to the field of ophthalmology and underscore the potential benefits of intra-operative Bevacizumab in managing macular edema. This study represents a significant step forward in understanding and improving outcomes for patients with macular edema, ultimately enhancing the quality of care in ophthalmic practice. However, further research and larger-scale studies are warranted to validate results of current study and to explore the long-term efficacy and safety of this intervention.

Limitations: The limited sample size of the study, consisting of just 60 individuals, may have implications for the generalizability of the findings and the statistical power achieved, which could potentially impact the reliability of the results. The follow-up period of three months post-surgery might not adequately capture long-term outcomes or potential complications associated with intra-operative Bevacizumab. Longer follow-up durations could provide insights into sustained efficacy and delayed adverse effects.

CONCLUSION

Administering intravitreal bevacizumab during phacoemulsification demonstrates superior outcomes in Best Corrected Visual Acuity and Optical Coherence Tomography for diabetic patients with macular edema who are undergoing cataract surgery.

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Authors Contributions:

Haider Ali Chaudhry: Study Conception and design, Data Acquisition, and Interpretation of results, revised, drafting manuscript and approved the manuscript

Gulnaz: Study design, data Acquisition, Data Analysis and Interpretation revised, drafting manuscript and approved the manuscript:

Irfan Ahmed Sualeh: Study design, Data analysis, writing manuscript, revised, and approved it

Muhammad Ahmad: Data collection, writing manuscript, revised, and approved it

All authors are equally responsible for integrity of research work

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