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ORIGINAL ARTICLE

Results of Intravitreal Injection of Bevacizumab before and with Phacoemulsification in Management of Diabetic Macular Edema in Cataractous Patients

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Abstract

Background: ***Ocular consequences of diabetes include cataracts and diabetic macular edema, the latter of which is the most common cause of visual impairment in diabetic individuals.***

Aim and objectives: ***To compare the efficacy and safety of phacoemulsification with injectable bevacizumab for diabetic macular edema to that of a staged procedure that begins with injectable bevacizumab and then proceeds to phacoemulsification using optical coherence tomography.***

Patients and methods: ***A prospective interventional research was carried out at Al-Azhar University Hospitals on 40 cataractous eyes with diabetic macular edema. All patients were separated into 2 groups: Group A, in which twenty eyes were managed by intravitreal injection of Bevacizumab 0.05ml (1.25mg) then underwent phacoemulsification after 2 weeks, and Group B, in which 20 eyes were managed by combined phacoemulsification & intravitreal injection of Bevacizumab 0.05ml (1.25mg) in the same session. After surgery, patients were monitored for 1 month, 2 months, and 3 months to record their CMT and best corrected visual acuity.***

Results: ***No statistically significant difference had been found among groups considering baseline CMT before operation, one and 2 months postoperative; however, the mean of CMT decreased significantly after 1 and 2 months in both staged and combined groups. No significant difference was found among both groups considering baseline BCVA before operation. The mean of BCVA increased significantly after one and two months in both groups.***

Conclusion: ***No significant difference among groups considering baseline CMT before operation, 1 and 2 months postoperative.***

Keywords: Diabetic; macular edema; Cataract; Bevacizumab; phacoemulsification

1. Introduction

Diabetes is a common disease that is growing in frequency. In 2019, 463 million adults worldwide, aged 20 to 79, were known to have diabetes.[1] The most frequent reason why diabetic people experience vision impairment is diabetic macular edema (DME). Research has shown that the release of soluble vascular and inflammatory mediators, such as pro-inflammatory cytokines and vascular endothelial growth factors, mediates the leakage of plasma components from the injured vasculature. Additionally, research revealed elevated VEGF levels in both the vitreous and aqueous phases, and these results can be related to the pathophysiology and severity of DME.[2] Another well-known ocular effect of diabetes is cataracts, for which people with diabetes may be responsible for upto twenty percent of cataract procedures. It has long been debatable whether cataract surgery accelerates diabetic maculopathy or retinopathy.[3] If diabetic macular edema is present during phacoemulsification, it should be treated before surgery because it is an unreliable indicator of visual recovery after surgery, according to Royal College guidelines. Research suggests that optical coherence tomography–detected diabetic macular edema may worsen by more than 30% during phacoemulsification. After phacoemulsification and intraocular IOL installation, the body produces a number of inflammatory chemicals, such as cytokines, vascular endothelial growth factors, interleukin 1, and epithelium-derived growth factors, which exacerbate diabetic macular edema. [4]

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The sterile operative area of cataract surgery offers the perfect environment for intravitreal drug administration. Since 2005, bevacizumab (Avastin) intravitreal injections have been used to treat neovascular and exudative ocular disorders. One intravitreal injection of 1.25 mg every four weeks is the recommended dosage. Bevacizumab can reach the retina's outermost layers. The drug has a vitreous half-life of 9.8 days and a plasma half-life of 17–21 days after being injected intravitreally. Macular thickness may be measured with great reproducibility using optical coherence tomography (OCT) in both healthy subjects and diabetic patients. It is an objective, non-invasive, non-contact, well-tolerated, and highly reproducible approach with an approximate 10μm resolution for quantitative measurements of retinal thickness. One well-known technique for examining the retina's architecture in vivo is OCT. The most crucial diagnostic prognostic technique for DME management is OCT. [5]

The purpose of this study is to compare the efficacy and durability of two different procedures for treating diabetic macular edema using optical coherence tomography: one that involves phacoemulsification and the other that begins with an intravitreal injection of bevacizumab.

2. Patients and methods

In our prospective interventional research, 40 cataractous eyes with diabetic macular edema were recruited from Al-Azhar University Hospitals from the beginning of April 2022 to the end of August 2023.

We included all patients with diabetes mellitus and visually significant cataracts with diabetic macular edema (CMT; 400 – 450 Mm). We excluded patients with proliferative diabetic retinopathy, previous retinal laser treatment or intraocular surgery, any intravitreal injection, complicated cataract surgery, or any other ocular diseases.

All patients were separated into 2 groups: Group A, in which 20 eyes were managed by intravitreal injection of Bevacizumab 0.05ml (1.25mg) and then underwent phacoemulsification after 2 weeks, and Group B, in which 20 eyes were managed by combined phacoemulsification and intravitreal injection of Bevacizumab 0.05ml (1.25mg) in the same session.

All patients had been subjected to history and clinical examination (including ocular surface, anterior chamber, crystalline lens, fundus examination, intra-ocular pressure measurement, and visual acuity test using Landolt c chart and converting log MAR) in addition to Conventional OCT imaging (3D OCT 2000Topcon Corporation, Tokyo, Japan). Using SS-OCT, macular and retinal thickness were evaluated. The type of macular edema, presence of subretinal fluid (SRF), and interruption of outer retinal were also assessed.

As regards phacoemulsification and intravitreal injection of Bevacizumab, 20 eyes were managed by intravitreal injection of Bevacizumab 0.05ml (1.25mg) then underwent phacoemulsification after 2 weeks in Group A. in Group B, 20 eyes were managed by combined phacoemulsification and intravitreal injection of Bevacizumab 0.05ml (1.25mg) in the same session. 0.1mL of a solution containing 1.25 mg of Bevacizumab (Avastin®; Genentech; California, United States) had been injected intravitreally via the sclera from 3.5mm posterior to the limbus in group B, the bevacizumab injection group, following cataract surgery.

Patients were followed postoperatively for recording the CMT measured on optical coherence tomography (3D OCT 2000 Topcon Corporation, Tokyo, Japan). & best corrected visual acuity at 1month, 2 months.

The Al-Azhar Faculty of Medicine's Ethics Committee approved this work. Before their involvement in this research, the studied cases or their families provided us with written informed consent.

STATISTICAL ANALYSIS

The following software was used: SPSS 25.0 (IBM Inc., Chicago, USA), Excel 2016 from Microsoft Office, and MedCalC 19.1. Were used to examine the collected data.

To ensure that the data followed a normal distribution, we employed the Kolmogorov-Smirnov test. Descriptive statistics were computed as follows: for numerical parametric data, it was mean ± SD (standard deviation) and minimum and maximum of the range. For numerical nonparametric data, it was median and first and third interquartile range. And for categorical data, it was number and percentage.

The independent t-test was employed for inferential studies when two separate groups possessed parametric data, and the Mann-Whitney U-test for nonparametric data. In order to do inferential analysis on qualitative data for separate groups, the chi-square test was utilized.

When testing for statistical significance among three time interval means, repeated ANOVA was employed, assuming that the data follows a normal distribution. Examples that are related To test for a statistically significant difference between the means of three time intervals in cases where the data is not normally distributed, Friedman's Two-Way Analysis of Variance by Ranks was employed. Assume that a significant difference exists with a p-value less than 0.05. The measurements within the group were compared pairwise, and the results

were adjusted using the Bonferroni correction for multiple testing. A significance level of 5% was used to evaluate the acquired results.

3. Results

Table 1. Demographic data of patients in both groups regarding age and gender.

DEMOGRAPHIC AND CLINICAL DATA	GROUP A (N = 20)	GROUP B (N = 20)	STATISTICAL TEST
GENDER N (%)			Chi-square test
MALE	9 (45 %)	8 (40 %)	$X^2 = 0.102$
FEMALE	11 (55 %)	12 (60 %)	P-value = 0.749 n.s.
AGE (YEARS)			t-test
(MEAN ± SD)	58.95 ± 6.43	58.2 ± 6.16	t = 0.377
MED. (MIN-MAX)	58.5 (50 - 70)	57.5 (49 - 69)	P-value = 0.71 n.s.

Our results showed that the age (y) of group A ranged from 50 to 70 with mean ± SD = 58.95 ± 6.43 while in group B the age (y) ranged from 49 to 69 with mean ± SD = 58.2 ± 6.16 with no statistically significant variation (p= 0.708) among the 2 groups. Regarding Gender, there had been no statistically significant difference among the two studied groups (p= 0.749).

Table 2. Clinical data of diabetes mellitus patients in both groups.

DEMOGRAPHIC AND CLINICAL DATA	GROUP A (N = 20)	GROUP B (N = 20)	STATISTICAL TEST
DIABETES STATUS N (%)			
CONTROLLED	4 (20 %)	4 (20 %)	
UNCONTROLLED	16 (80 %)	16 (80 %)	
DIABETIC DISEASE DURATION			t-test
MEAN ± SD	14 ± 3.13	14.95 ± 2.87	t-value = 1.0
MED. (MIN-MAX)	14 (9 - 20)	14 (10 - 20)	P-value = 0.377 n.s.
OTHER SYSTEMIC DISEASES			Chi-square test
NO	14 (70 %)	9 (45 %)	$X^2 = 2.56$
HTN	6 (30 %)	11 (55 %)	P-value = 0.11 n.s.
COMPLAINT			
DROP OF VISION	20 (100 %)	20 (100 %)	
MANAGEMENT			
STAGED	20 (100 %)	-	
COMBINED	-	20 (100 %)	

Our results showed that diabetes duration (y) in group A ranged from 5 to 16 with mean ± SD = 10.75 ± 3.51 while in group B the Diabetes duration (y) ranged from 4 to 20 with mean ± SD = 11.25 ± 4.85 with no statistically significant difference (p= 0.711) among the 2groups & no statistical significant difference among the 2 studied groups (p= 0.705) as regard diabetes status, diabetic disease duration and Other systemic diseases.

Table 3. Central macular thickness (CMT) (µm) at baseline (before operation) & post-operation at 1 and 2 months in both groups.

CMT	GROUP A STAGED (N = TWENTY)	GROUP B COMBINED (N = TWENTY)	INDEPENDENT T-TEST t-value	p-value
BEFORE (MM)	420.7 ± 19.63[a]	426.95 ± 18.22[a]	1.04	0.303 ns
(BASELINE)	413 (390 - 460)	426 (398 - 470)		
AFTER 1M (MM)	413.2 ± 19.85[b]	418.7 ± 15.68[b]	0.973	0.337 ns
	407.5 (385 - 455)	419 (399 - 462)		
AFTER 2M (MM)	410.8 ± 19.73[c]	416.7 ± 15.73[c]	1.04	0.303 ns
	405 (382 - 450)	415.5 (396 - 460)		
ONE WAY	F-value = 143.5	F-value = 61.0		
REPEATED ANOVA	p-value < 0.001	p-value < 0.001		

One-way repeated ANOVA indicated that the mean of CMT decreased significantly after 1, and 2 months compared with baseline (before operation) in both staged and combined groups ($p<0.001$). Nonetheless, the t-test revealed no significant difference among the two groups considering baseline CMT before the operation, one and 2 months postoperative (P-value= 0.303, 0.337 & 0.303 respectively). Our results showed that CMT at one-month follow-up (µm) in group A ranged from 385 to 455 with mean ± SD = 413.2 ± 19.85 while in group B the CMT at one-month follow-up (µm) ranged from 399 to 462 with mean ± SD = 418.7 ± 15.68 with no statistically significant difference (p= 0.337) among the 2groups. CMT at two months follow-up (µm) in group A ranged from 382 to 450 with mean ± SD = 410.8 ± 19.73 while in group B the CMT at two months follow-up (µm) ranged from 396 to 460 with mean ± SD = 416.7 ± 15.73 with no statistically significant difference (p = 0.303) among the two groups.

Table 4. Best-corrected visual acuity (BCVA) (LogMAR) at baseline (before operation) & post-operation at 1 and 2 months in both groups.

BCVA	GROUP A STAGED (N = TWENTY)	GROUP B COMBINED (N = TWENTY)	MANN-WHITNEY U TEST	
			M-W U	p-value
BEFORE (LOGMAR)	0.1 ± 0.05[a]	0.11 ± 0.05 [a]	165.0	0.321 ns
	0.1 (0.02 - 0.16)	0.1 (0.05 - 0.2)		
AFTER 1M (LOGMAR)	0.39 ± 0.07[b]	0.38 ± 0.12 [b]	182.0	0.611 ns
	0.4 (0.3 - 0.5)	0.35 (0.2 - 0.6)		
AFTER 2M (LOGMAR)	0.3 ± 0.07[c]	0.34 ± 0.12 [b]	157.0	0.221 ns
	0.3 (0.2 - 0.5)	0.4 (0.2 - 0.6)		
FRIEDMAN'S TWO-WAY ANOVA	Test -value = .38.7	Test -value = .35.18		
	p-value < 0.001	p-value < 0.001		

One-way repeated ANOVA indicated that the BVCA was significantly increased after 1, and 2 months compared with baseline (before operation) in both staged and combined groups (p<0.001). In the staged group BCVA after 2 months decreased significantly compared with BCVA after 1 month, on the other hand in the combined group BCVA after 2 months decreased compared with BCVA after 1 month but this decrease was not statistically significant.

a t-test revealed no significant difference among the 2groups considering baseline BCVA before operation, one and 2 months postoperative (P-value= 0.321, 0.611 & 0.221 respectively)

Regarding best-corrected visual acuity (BCVA) (LogMAR) among the study population. Our results showed that BCVA at one-month follow-up (LogMAR) in group A ranged from 0.3 to 0.5 with mean ± SD = 0.39 ± 0.07 while in group B the BCVA at one-month follow-up (LogMAR) ranged from 0.2 to 0.6 with mean ± SD = 0.38 ± 0.12 with no statistically significant difference (p = 0.611) among the two groups.

4. Discussion

People with diabetes are at risk of developing diabetic retinopathy (DR). Diabetes mellitus is a worldwide disease. At primary care screening, DME is the most common reason for vision-threatening DR in individuals with diabetes, affecting about one in ten of these patients. In studied cases with diabetes, cataracts, and clinically significant macular edema are prominent reasons for reduced vision. [6]

DME management is complicated, and different treatment modalities are frequently required. Even though there is currently excitement surrounding the evaluation of several novel treatments for DME, such as intravitreal pharmacologic therapy (such as corticosteroids anti-VEGF medications), laser photocoagulation is still the gold standard in DME.[7]

In addition to laser photocoagulation treatment, anti-VEGF therapy has emerged as a major therapeutic option for DME. For this reason, Bevacizumab is a commonly used medication. In certain cases, intravitreal injection is done in conjunction with cataract surgery for the convenience of the patient. Numerous studies have shown that intravitreal bevacizumab injection, when combined with cataract surgery, is a more effective way to prevent the advancement of diabetic retinopathy than cataract surgery alone.[8]

Our study aimed to assess the improvement and stability of diabetic macular edema after phacoemulsification combined with intravitreal injection of Bevacizumab compared to a staged procedure started by intravitreal injection of Bevacizumab followed by phacoemulsification, as measured on optical coherence tomography.

Our study was conducted on 40 cataractous eyes with diabetic macular edema. All patients were separated into 2 groups: Group A included 20 eyes managed by intravitreal injection of Bevacizumab 0.05ml (1.25mg) and then undergoing phacoemulsification after 2 weeks, and Group B included 20 eyes managed by combined phacoemulsification and intravitreal injection of Bevacizumab 0.05ml (1.25mg) in the same session.

Our results were supported by Kwak et al.[8] Their results showed that the mean of diabetes duration had been 13.1 ± 7.71. There were no significant differences regarding diabetes duration among the studied groups.

Takamura et al.[9] supported our results. Their results showed no significant differences regarding systemic diseases.

Our outcomes were supported by Akinci et al.[10] Their results showed that the first CMT ranged from 302 to 487 μm, with a mean of 387.5 ±101.5. In the initial and 3rd months following the operation, the mean CMT was 292.7 ±57.2 μm (with a range of 241–312 μm) and 275.5 ± 40.3 μm (with a range of 239–265 μm), respectively. The CMT obtained during the first and third months following the procedure had been considerably less than the CMT at the beginning (P <0.001, P <0.001). In every eye, the central macular thickness dropped.

Furthermore, in a meta-analysis by Feng et al.[11] They found that the IVB groups' central macular thickness was considerably smaller than the control groups' at three and six months following surgery (P = 0.01, P = 0.0004, & P = 0.01, respectively). Their research validated our findings.

Our results were supported by Akinci et al.[10]

Their results showed that Initial BCVA (decimal equivalents of Snellen acuities) ranged from 0.05 to 0.2, with a mean of 0.10 ±0.04 (SD). The BCVA values obtained at one and three months following the procedure were 0.4 ± 0.16 (SD) (0.2–0.5) and 0.5 ± 0.12 (SD) (0.3–0.6), in that order. P = 0.004 & P = 0.003, respectively, indicated that the initial BCVA had been considerably higher than the BCVA in the first and 3rd months following the surgery.

Moreover, our results were supported by Khodabandeh et al.[12] Their finding showed that the mean initial BCVA in the bevacizumab group was 0.54 ± 0.21. The BCVA in the bevacizumab group recorded in the 1st and third months after the surgery was 0.07 ± 0.06 (SD) and 0.06 ± 0.04 (SD), respectively. There were significant differences regarding BCVA among the studied groups.

Moreover, our results were in contrast with those of ul Hassan et al.[13] who aimed to assess the effectiveness of a single intravitreal Bevacizumab injection for the management of postoperative reduction in vision in patients with DME, either during or immediately after cataract surgery. Their research comprised 60 eyes of 60 patients who had diabetic macular edema. Their results showed that bevacizumab-treated eyes showed no significant change.

4. Conclusion

Combined phacoemulsification and intravitreal injection of Bevacizumab 0.05ml (1.25mg) in the same session was not significantly different from the intravitreal injection of Bevacizumab 0.05ml (1.25mg) then undergoing phacoemulsification after 2 weeks in the improvement & stability of diabetic macular edema.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

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