



EFFECT OF PHACOEMULSIFICATION ON THE PROGRESSION OF DIABETIC RETINOPATHY AND DIABETIC MACULAR EDEMA

Ophthalmology

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ABSTRACT

Background: DR is the leading cause of vision loss in adults aged 22-74 years. DR ranked as the fifth most common causes of preventable blindness. In cataract surgery, blood aqueous barrier is impaired leading to an increased risk of post-operative inflammation and development of a sight-threatening macular edema in diabetics with or without evidence of diabetic retinopathy. The study described herein is to investigate the effect of phacoemulsification surgery on the progression of diabetic retinopathy and diabetic macular edema after phacoemulsification cataract surgery.

Material And Methods: A randomized control trial was conducted in the Department of Ophthalmology, RIMS, Imphal, Manipur for a period of 24 months with effect from September 2017 to August 2019 among 50 patients aged between 18 to 80 years with type 2 diabetes mellitus admitted for phacoemulsification surgery to determine the effect of phacoemulsification on the progression of diabetic retinopathy and diabetic macular edema. Patient's diabetic retinopathy and Diabetic macular edema were graded using Early Treatment Diabetic Retinopathy Study criteria pre and post operatively. The results were tabulated and statistically evaluated using proper methods.

Results: There was significant improvement in the visual acuity after cataract surgery for all levels of preoperative retinopathy. Progression of retinopathy was seen in 10% case eye and 8% in fellow control group which was comparable in both the groups. The finding was statistically insignificant ($p > 0.05$). In only 2% of the patient diabetic macular edema developed at 6 month follow-up.

Conclusion: Phacoemulsification cataract surgery does not cause acceleration of diabetic retinopathy and diabetic macular edema post operatively and any progression that is observed probably represents the natural course of the disease rather than being a direct effect of surgery.

KEYWORDS

Cataract, Diabetic Retinopathy, Diabetic Macular Edema.

INTRODUCTION

The prevalence of diabetes mellitus (DM) is increasing on a daily basis, with a estimation that there will be 439 million DM patients by 2030.¹ Cataracts, specially with cortical and posterior sub capsular opacities are three to four times more prevalent in diabetic patients under the age of 65 and cataracts are twice as prevalent in patients over 65. Accumulation of sorbitol and advanced glycation end products in the lens is one of the mechanisms of diabetic cataract development. The main risk factors for developing diabetic retinopathy (DR) are longer duration of diabetes and poor metabolic control.² Diabetic retinopathy (DR) and diabetic macular edema (DME) are common micro vascular complications in diabetic patients and may have a sudden and debilitating impact on visual acuity (VA), eventually leading to blindness. From 1990 to 2010, DR was the fifth most common cause of preventable blindness and fifth most common cause of moderate to severe visual impairment. In 2010, of an estimated 285 million people worldwide with diabetes, over one-third have signs of DR, and a third of these patients are suffering from vision-threatening diabetic retinopathy (VTDR) which is defined as severe non-proliferative DR or proliferative DR (PDR) or the presence of diabetic macular edema (DME).³ The Diabetes Control and Complications Trial (DCCT) reported that 27% of type 1 diabetic patients developed macular edema within 9 years from the onset of diabetes. Few studies indicate that in patients with type 2 diabetes, the prevalence increases from 3% within 5 years of diagnosis to 28% after 20 years duration. In about 33–35% of patients, there is spontaneous resolution of macular edema after 6 months if left untreated. Early Treatment of Diabetic Retinopathy Study (ETDRS) guidelines are used to characterize the severity of macular edema and for treatment purpose in clinically significant macular edema (CSME) as an equivalent of DME. The pathogenesis includes the existence of chronic hyperglycemia, accumulation of free radicals, AGE proteins, protein kinase C (PKC) formation, activation of vascular endothelial growth factors (especially VEGF-A) which increase vascular permeability.⁴ Cataract surgery is usually performed in patients with diabetic mellitus before

significant diabetic retinopathy develops and before the cataract becomes too dense. The progression of DR after intracapsular (ICCE) and extracapsular (ECCE) cataract extraction is well documented.⁵ The progression of DR and diabetic macular edema after cataract surgery may be enhanced by the breakdown of the blood-retinal barrier (BRB) or enhanced inflammation in diabetic patients which may be associated with iatrogenic prostaglandins production. The smaller incision size and shorter surgical time of phacoemulsification cause less breakdown of BRB, which may result in decreased surgical inflammation.⁶ The development of DR and its complications after introduction of phacoemulsification is poorly described, as there is development of new materials for intraocular lenses (IOLs) that decrease inflammatory activity. It has been demonstrated that DR progresses in approximately 10-30% of patients after cataract surgery, although some authors have hypothesized that the progression of DR after cataract surgery is due to the natural course of the condition which is independent of the surgery.⁷ Diabetic macular edema has been shown to worsen after cataract surgery, although controversy remains as to be its direct or indirect effect on the progression. Therefore, the purpose of the study described herein is to investigate the effect of phacoemulsification surgery on the progression of diabetic retinopathy and diabetic macular edema in diabetic patients with or without diabetic retinopathy and diabetic macular edema.

MATERIALS AND METHODS

A randomized control trial was conducted in the Department of Ophthalmology RIMS, Imphal, Manipur for a period of 24 months with effect from September 2017 to August 2019 among patients aged between 18 to 80 years with diabetes mellitus admitted for phacoemulsification surgery to determine the effect of phacoemulsification on the progression of diabetic retinopathy and diabetic macular edema in patients with type 2 diabetes mellitus. Ethical approval from the institution and informed consent from the patients were taken before the initiation of the study. A total 50 patients with diabetic mellitus were included in this study who had undergone

phacoemulsification. Exclusion criteria were history of cataract surgery in the fellow eye within the previous 12 months, DME or focal or grid photocoagulation of a previous macular edema before surgery, macular ischemia on fluorescein angiography, rubeosis iridis or neovascular glaucoma, maculopathies, chronic glaucoma, optic disc atrophy, myopia over -7.00D, history of ocular inflammatory episodes. Study variables were age, sex, religion, occupation, education, socio-economy condition, address, marital status, duration of surgery. Operated eye is taken as case and contralateral non operated eye until 1 year is taken as control group. A patient's diabetic retinopathy and Diabetic macular edema were graded using Early Treatment Diabetic Retinopathy Study criteria. A complete medical history and ocular examination including dilated fundus examinations were done before surgery for all the patients and status of retinopathy and maculopathy in both eyes were noted using slit lamp biomicroscopy, direct ophthalmoscope, indirect ophthalmoscope. OCT imaging was performed for all patients. In patients where view of the retina was obscured by the lens opacity, the preoperative retinopathy status was assumed to be that recorded on the first postoperative day. All the operated patients were examined at post-operative day 1, 1 month, 3 month and at 6 months after surgery. At each review the Snellens visual acuity, grade of retinopathy and macular edema in both eyes are recorded. Outcomes were assessed 6 months postoperatively and included visual acuity (VA), progression of retinopathy and incidence of macular edema (referring to optical coherence tomography). Progression of retinopathy and incidence of DME were compared to the non-operated fellow eyes. Post-operative progression of DR was to be considered to have occurred if patient with no DR before surgery developed DR or patient with pre-existing DR had a progression of an increased level of retinopathy or development or progression of maculopathy to clinical significance.

Statistical analysis was done using SPSS version 21 software. Mean percentage and proportions were used for descriptive statistics. Chi square test, ANOVA and t-test were used for categorical variables.

RESULTS

A total 50 cases were included in this study satisfying inclusion and exclusion criteria over a period of 24 months from September 2017 to August 2019. Majority of the patients were from the age group of 56-65 years of age (44%). Mean age was 65.6 years. Majority of the patients were from urban areas in 66% (33 out of 50) of cases. The mean duration of diabetes among the patients was 6.4±4.3 years and median was 7.0 (1-18) years.

Table 1: Distribution of respondents by HbA1c at various time interval

Time interval	HbA1c
Baseline	7.33±1.7
3rd month	6.95±1.4
6th month	7.0±1.6
Repeated measure ANOVA	F=3.546 p=0.055

According to the above table, baseline HbA1C was 7.33±1.7, at 3 months 6.95±1.4, at 6 months 7.0±1.6 respectively.

Table 2: Distribution of respondents by baseline preoperative BCVA in logMAR unit.

Case/control	Preoperative BCVA Mean ±SD	Paired t-test
Case	0.74±0.33	Value=6.792 df=49 p=0.000
Controls	0.48±0.28	

The mean pre-operative BCVA of case was 0.74±0.34 and for the control was 0.48±0.28. (logMAR unit).

Table 3: Distribution of respondents by baseline fundus finding of case and control eyes

Baseline fundus finding	Case n(%)	Control n(%)	Chi-square test
No DR	36(72.0)	35(70.0)	Value=0.073 df=2 p=0.964
Mild NPDR	8(16.0)	9(18.0)	
Moderate NPDR	6(12.0)	6(12.0)	

Severe NPDR	0	0
Total	50(100.0)	50(100.0)

No patient had pre-operative DME. Retinopathy was present in 28% of the cases and 30% of the controls. 72% cases had no form of retinopathy before surgery and 70% controls had no retinopathy before surgery.

Regarding baseline fundus findings, there was not much difference between case and control eye and the finding was statistically insignificant (p>0.05).

Table 4: Distribution of respondents by fundus finding at various times of control eye

Fundus finding of controls	Baseline n(%)	1 st month n(%)	3 rd month n(%)	6 th month n(%)	Chi-square test (yates corrected)
No DR	36(72.0)	36(72.0)	33(66.0)	32(64.0)	Value=0.34 8 p=0.999
Mild NPDR	8(16.0)	8(16.0)	10(20.0)	10(20.0)	
Moderate NPDR	6(12.0)	6(12.0)	6(12.0)	7(14.0)	
Sever NPDR	0(0.0)	0(0.0)	1(2.0)	1(2.0)	
Total	50(100.0)	50(100.0)	50(100.0)	50(100.0)	

Fundus findings of control eye didn't change till 1st month but at the end of 6th month, in 8% of the control eye DR was progressed. The finding was statistically insignificant (p>0.05).

Table 5: Distribution of respondents by fundus finding at various times of case eye

Fundus finding of cases	Baseline n(%)	1 st month n(%)	3 rd month n(%)	6 th month n(%)	Chi-square test (yates corrected)
No DR	36(72.0)	35(70.0)	33(66.0)	31(62.0)	Value=1.2 63 p=0.998
Mild NPDR	8(16.0)	9(18.0)	10(20.0)	11(22.0)	
Moderate NPDR	6(12.0)	6(12.0)	6(12.0)	7(14.0)	
Severe NPDR	0(0.0)	0(0.0)	1(2.0)	1(2.0)	
Total	50(100.0)	50(100.0)	50(100.0)	50(100.0)	

Progression of Diabetic Retinopathy was observed in 4 cases (10%) at the end of 6 months post-operative follow-up visit. The changes in fundus findings was statistically insignificant (p>0.05).

Table 6: Relation between case eye and control eye regarding fundus finding at various times

Fundus finding	1 st month		3 rd month		6 th month	
	Case n(%)	Control n(%)	Case n(%)	Control n(%)	Case n(%)	Control n(%)
No DR	35 (70.0)	36(72.0)	33(66.0)	33(66.0)	31(62.0)	32(64.0)
Mild DR	9(18.0)	8(16.0)	10(20.0)	10(20.0)	11(22.0)	10(20.0)
oderate DR	6(12.0)	6(12.0)	6(12.0)	6(12.0)	7(14.0)	7(14.0)
Severe NPDR	0(0.0)	0(0.0)	1(2.0)	1(2.0)	1(2.0)	1(2.0)
Total	50(100.0)	50(100.0)	50(100.0)	50(100.0)	50 (100.0)	50 (100.0)
Chi-square test (yates)	Value=0.073 Df=2 p=0.964	Value=0 Df=3 p=1.0	Value=0.0 Df=3 p=0.99			

At the end of 6 months follow-up after phacoemulsification surgery, progression of diabetic retinopathy found in 10% eyes of the case group and in 8% eyes from the control group respectively.

Table 7: Pre- and post- operative BCVA of cases and controls (logMAR Unit)

Interval	BCVA Case Mean ±SD	BCVA Control Mean ±SD
Preoperative	0.74±0.33	0.48±0.28
1 st month	0.18±0.22	0.36±0.31

3 rd month	0.14±0.23	0.47±0.28
6 th month	0.16±0.30	0.54±0.30
Repeated measure ANOVA	F=88.144 p=0.000	F=8.253 P=0.056

The mean pre-operative baseline visual acuity of case was 0.74±0.33 (log MAR unit) and 0.16±0.30 at 6 months (statistically significant). Visual acuity increases by 3 to 4 lines in 94.5% of the cases (statistically significant).

Table 8: Macular thickness among cases and controls in pre and post-operative follow-up visits.

Interval	CMT Case Mean ±SD	CMT Control Mean ±SD
Preoperative	188.0±16.2	188.1±16.1
1 st month	190.3±17.0	188.2±16.1
3 rd month	197.5±17.9	189.4±17.5
6 th month	193.7±22.2	190.2±22.4
Repeated measure ANOVA	F=44.8 p=0.000	F=2.670 P=0.058

The mean pre-operative central macular thickness of cases was 188.0±16.2µm, increases to 190.3±17.0µm at post-operative 1 month and 197.5±17.9µm at 3 month post-operative follow up (significant), then decreases to 193.7±22.2µm at 6 months but not near to baseline. Development of diabetic macular edema was observed in one patient (2%) which required treatment.

increase in the mean central macular thickness was also observed among the control eyes at 6th month follow up visit which was statistically insignificant.

DISCUSSION

Many studies already documented about the progression of Diabetic Retinopathy and Diabetic macular edema after ICCE and ECCE. Few studies have shown contradictory results on the progression of DR after the introduction of phacoemulsification for cataract surgery. These discrepancies may be due to the different methodology used to study postoperative progression of DR. Thus, many authors report that cataract surgery increases the risk of DR progression as an independent risk factor. Others state that the patient's metabolic status and the surgeon's experience are more important than the effect of surgery in the progression of DR and DME after cataract surgery.

This study methodology was similar to that in many studies, in which surgery was performed in one eye and the other fellow eye was taken as control.

The mean age of the study population was 65.6±8.0 years, and all the patients were type 2 diabetic patients with a mean duration of diabetes of 6.4±4.3 years. Majority of the patients were from urban area constitutes 66% and majority were female patients. Gender, duration of diabetes, and mean HbA1c were not significant influencing factors with respect to final post-operative visual outcome.

There was significant improvement in the visual acuity after cataract surgery for all levels of preoperative retinopathy. Visual acuity increased 3 or more lines in 94% of the patient at the end of 6 months follow up visit which is comparable with the study conducted by Hoda M et al³⁰ (90%). The mean postoperative visual acuity at the final follow-up visit was 0.16±0.3 (p=0.000) which was statistically significant. In 2 patients (4%) there was no change in the visual acuity and in 2% of cases visual acuity was worsen.

Progression of retinopathy was seen in 18% of eyes in this study which is comparable with study conducted by Pedro RA et al³³ (21%). This percentage is lower than that seen in many recent series of phacoemulsification in diabetic patients. Mittra RA et al³⁹ reported that 25% patients had progression of DR with 6 to 10 months of follow up. Hoda M et al³⁰ found that there was progression of DR in 10% of the cases. However, comparison between studies with different populations and level of preoperative retinopathy are problematic. In the present study, the progression of DR was similar in the operated eyes and the fellow control eyes (10% and 8% respectively). There was no statistically significant difference in the number of operated and fellow eyes that had evidenced of progressive retinopathy (p=). The progression was symmetrical in both eyes in 5 patients. In 4 patients

DR progressed in the operated case eye only and in 1 (2%) patient it progressed in the fellow control eye only.

The risk factors for the progression of DR in the present study were duration of diabetes mellitus and high level of HbA1c which was resulting from poor metabolic control of diabetes mellitus. Many studies implicate poor metabolic control of diabetes mellitus in the progression of DR and DME after cataract surgery. Squarrel D et al²⁹ reported that it is the only risk factor for the progression of DR. Hauser D et al⁴¹ reported that the occurrence and progression of DR after phacoemulsification were associated with different factors and poor systemic control of diabetes increases the risk.

The study of diabetic macular edema after cataract surgery is difficult because it must be differentiated from pseudophakic CME. Macular edema tends to progress when caused by diabetes and resolves when caused by Irvin-Gass syndrome. Patients in whom macular edema was not detected before the surgery and who developed it in the postoperative period pose a challenge; whether it is the edema due to the result of Irvin-Gass syndrome or evolving diabetic maculopathy. Fluorescein angiography may help to make the decision in this condition.

In this study, the mean preoperative central macular thickness of operated eye was 188.6±16.2 µm which is gradually increased postoperative follow-up at 1 month (190.3±17.9µm) till 197.5±17.9 µm at postoperative 3 month. Then the mean central macular thickness decreased to 193.7±22.2 µm at 6 months follow up but not near to the preoperative baseline value. This results agree with previous studies by Patel JI et al⁴⁰ and Jurecka T et al⁴³. Similar to the result of the present study, Hayanshi K et al³⁵ postulated that the degree of diabetic macular edema generally worsens after cataract surgery but macular edema that occurs after cataract surgery resolves spontaneously.

CONCLUSION

Phacoemulsification cataract surgery does not cause acceleration of diabetic retinopathy post operatively and any progression that is observed probably represents the natural course of the disease rather than being a direct effect of phacoemulsification surgery.

Although macular edema was common after cataract surgery, it often followed a benign course. Mean foveal thickness increases after phacoemulsification which was evident during post operative one month and continued till three months, then decreased. Altered concentration of angiogenic and anti-angiogenic growth factors after cataract surgery may induce subclinical worsening of diabetic macular edema. According to the result of this study, phacoemulsification surgery does not cause progression of diabetic macular edema.

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