Outcome of Phacoemulsification without Anti-vascular Endothelial Growth Factor in Patients with Treatment Naïve Diabetic Retinopathy

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ABSTRACT

Introduction: This retrospective, non-randomized, observational study was conducted at ASG Eye Hospital, Kathmandu to evaluate the outcome of phacoemulsification without anti-Vascular Endothelial Growth Factor (VEGF) in patients with treatment naïve diabetic retinopathy.

Materials and methods: Records of all patients who underwent phacoemulsification without Bevacizumab in treatment of naïve patients with any grade of non-proliferative Diabetic Retinopathy (NPDR) were seen. Pre-operative and post-operative visual acuity along with central macular thickness (CMT) was compared.

Results: The study comprised 32 eyes of 20 patients with treatment naïve non-proliferative Diabetic Retinopathy who underwent phacoemulsification. Twelve were men and eight were women with an average age of 69.2 years (range 55 years to 83 years). The average preoperative central macular thickness as measured on optical coherence tomography was 254.63± 20.25 microns and 1-month postoperative central macular thickness was 254.72± 19.96 microns; the study did not find any significant difference (p-value 0.918). The average difference in the central macular thickness between the 1-month postoperative and preoperative values was 0.09 microns.

Conclusion: Uneventful phacoemulsification in eyes with treatment naïve diabetic retinopathy does not cause an increase in central macular thickness after surgery and thus anti-Vascular Endothelial Growth Factor as an adjunct is not mandatory.

Key words: Anti-VEGF, Bevacizumab, Cataract, Diabetic macular edema, Diabetic retinopathy, Preventable blindness, Phacoemulsification.

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INTRODUCTION

The burden of diabetes mellitus (DM) is a global problem. It is estimated that 700 million people will have DM by 2045(Saeedi et al., 2019). Due to this increasing prevalence of diabetes and the limitation of healthcare providers in developing countries like Nepal, it becomes a major challenge for treating physicians to manage diabetes and its known complications like nephropathy, peripheral neuropathy and retinopathy.

Diabetic retinopathy (DR) contributes to being one of the leading causes of preventable blindness worldwide. The causes of poor vision in patients with DR are macular edema (ME), vitreous hemorrhage (VH), and tractional or combined retinal detachment (RD) which may require lasers, injections, and surgery. In the past, focal or grid lasers were the mainstay of treatment in diabetic macular edema (DME). There has been a paradigm shift in managing DME since anti-VEGFs were introduced which gave better results than lasers (Bressler et al., 2018). Bevacizumab is an anti-VEGF agent that is approved for the treatment of disseminated colorectal cancer although not FDA-approved for intraocular use. But in developing countries like Nepal, Bevacizumab (Avastin) continues to be the most common and preferred anti-VEGF (Rijal et al., 2021).

Cataract is another major cause of preventable blindness especially in a developing country like Nepal (Brilliant et al., 1985). Even though there has been a tremendous development in the eye health sector in our country, significant lag continues to persist in rural areas where patients wait for the expected surgical eye camps to get operated. The modern approach to managing cataract is phacoemulsification and implantation of intraocular lens (IOL).

Diabetes further increases the risk of developing cataract by 2 to 4 times (Menchini et al., 2003). With the increasing prevalence of diabetes, the co-existence of DR and cataract is expected to increase over the next few decades. The outcome of cataract surgery in eyes with no other pre-existing intraocular conditions is good but predicting the outcome in eyes with pre-existing DR remains a challenge. A longer duration of diabetes and poor metabolic control contribute to an increased risk of postoperative complications.

Some studies (Squirrell et al.,2002; Krepler et al.,2002; Liu et al., 2015) have shown that operating patients with cataract and DR results in an increase in CMT and progression of DR, with sub-optimal visual outcomes. Prophylaxis with anti-VEGF injection has resulted in better outcomes in some studies (Takamura et al., 2009; Zhao et al., 2019). whereas other studies suggest the contrary (Mittra et al., 2000; Chung et al., 2002; El-Sobky et al., 2014). Hence, intravitreal injection of anti-VEGF during cataract surgery in eyes with DR remains a matter of confusion for ophthalmologists.

Therefore, this study was conducted to evaluate the CMT changes in the early postoperative course of 30 days in subjects with different grades of NPDR after uncomplicated phacoemulsification.

MATERIALS AND METHODS

This retrospective, non-randomized, observational study was done at ASG Eye Hospital, Kathmandu. Approval was taken

from the medical board of the hospital. All the surgeries were done by a single experienced surgeon. Records of all treatment naïve patients with DR who underwent phacoemulsification without Bevacizumab (Avastin) were reviewed. Eyes were graded into mild, moderate, severe, or very severe NPDR based on the Early Treatment Diabetic Retinopathy Study (ETDRS) grading scale. Those patients who had undergone OCT pre-operatively and one month postoperatively were included in the study. Patients with any macular pathology or any pre-existing intra-ocular conditions that could contribute to poor vision were excluded. Pre-operative and Post operative CMT at one month were measured on the mapping protocol of the Optovue OCT software (version 6.9).

RESULTS

Table 1: Details of all 32 eyes showing the grade of NPDR, pre-operative and post-operative (30 days) CMT.

S.N.	Age	Sex	Eye	Diabetes grading (NPDR)	PRE-OP CMT	POST-OP CMT (30 DAYS)
1	68	M	OD	Mild	245	251
2	68	M	OS	Mild	253	254
3	78	F	OD	Moderate	276	278
4	78	F	OS	Moderate	205	208
5	56	F	OD	Moderate	252	251
6	56	F	OS	Moderate	251	257
7	59	F	OD	Mild	258	251
8	59	F	OS	Mild	254	262
9	73	M	OD	Mild	263	260
10	83	M	OD	Moderate	230	238
11	83	M	OS	Mild	274	270
12	70	F	OD	Moderate	274	270
13	70	F	OS	Severe	262	262
14	67	F	OD	Mild	229	231
15	65	M	OD	Severe	264	257
16	55	M	OD	Moderate	241	239
17	55	M	OS	Moderate	225	230
18	78	M	OD	Severe	271	265
19	78	M	OS	Very severe	276	282
20	66	M	OD	Mild	294	297
21	78	F	OS	Mild	232	225
22	73	M	OD	Mild	242	249
23	73	M	OS	Moderate	263	260
24	74	F	OS	Mild	271	268
25	65	M	OD	Mild	249	258
26	65	M	OS	Mild	262	263
27	72	M	OD	Moderate	276	271
28	72	M	OS	Moderate	268	260
29	71	M	OD	Mild	235	234
30	71	M	OS	Moderate	215	208
31	78	F	OD	Severe	268	271
32	78	F	OS	Moderate	270	271

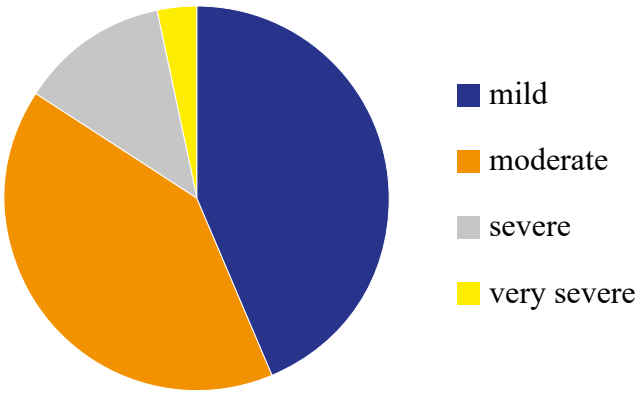

Figure 1: Distribution of diabetes grading among all 32 patients.

In this study, there were 32 eyes of 20 patients with different grades of non-proliferative diabetic retinopathy (NPDR) who underwent phacoemulsification without prior retinal LASER and/or intravitreal injection of anti-VEGF agents. Out of 20 patients, 12 were men and 8 were women. The average age was 69.2 years (ranging from 55 years to 83 years).

There were 14 eyes with mild NPDR, 13 eyes with moderate NPDR, 4 eyes with severe NPDR, and 1 eye with very severe NPDR.

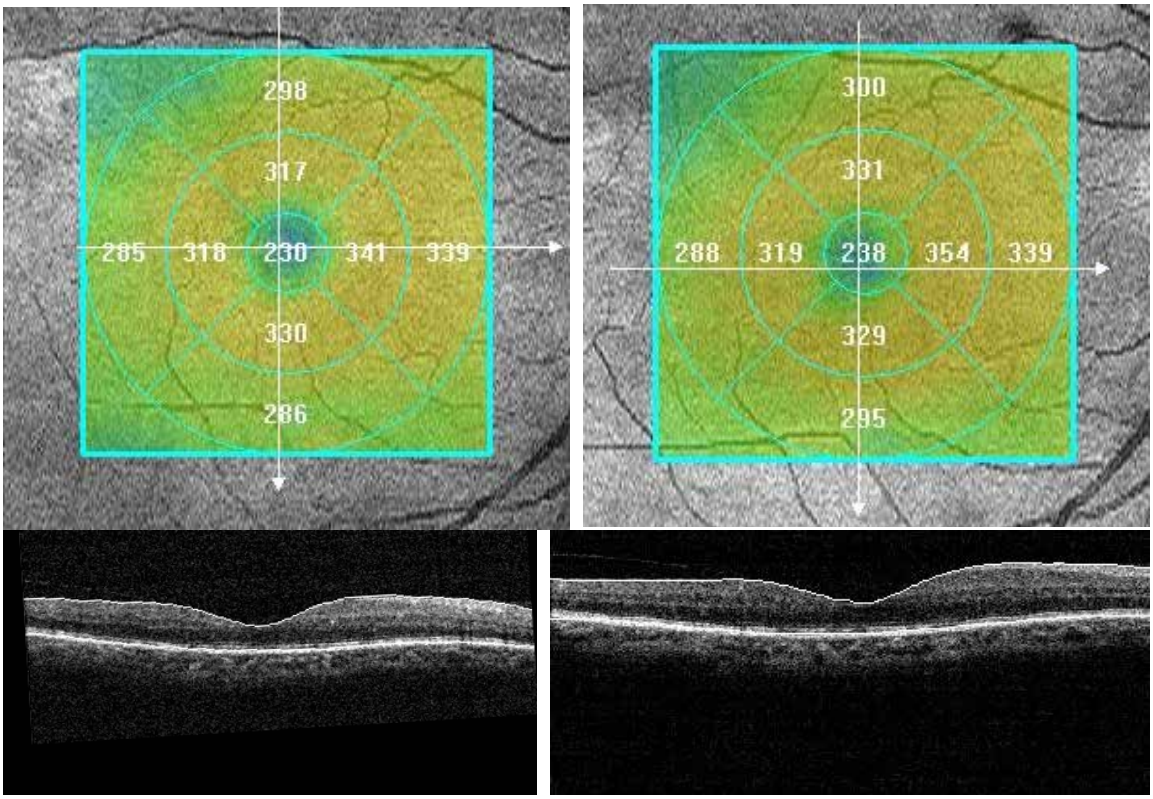

Figure 2: OCT image and macular thickness of the right eye of an 83-year-old male.
Figure 2(a), (b): Pre-operative measurements.
Figure 2(c), (d): Post-operative (POD-30) measurements.

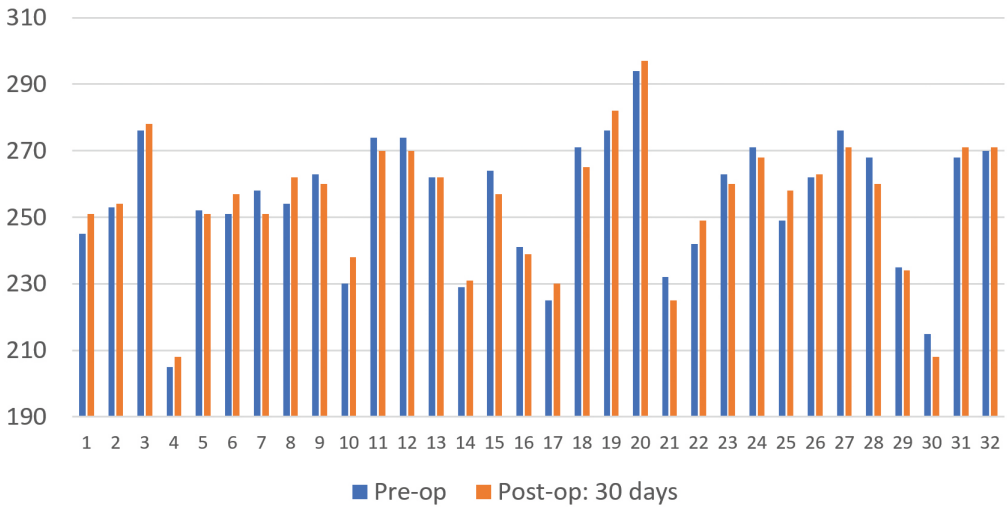

Figure 3: Comparative pre-operative and post-operative CMT (30 days) (Y-axis) of all 32 eyes (numerically arranged in X-axis).

The average preoperative central macular thickness (CMT), measured via the readings extracted from ocular coherence tomography (OCT) of the macula, was 254.63 ± 20.25 microns and 1-month post-operative CMT was 254.72± 19.96 microns. The average difference in the CMT between the 1-month postoperative and preoperative values was 0.09 microns.

Paired t-test was used to calculate the significance which yielded a p-value of 0.918, which is not statistically significant. Hence, there was no significant increase in CMT after phacoemulsification.

DISCUSSION

The approach to cataract with DR is variable depending on the eye care setup, ranging from SICS to Phacoemulsification with or without anti-VEGFs. The outcome of SICS and phacoemulsification is comparable in eyes without any other pre-existing intraocular pathology (Ruit et al., 2007). But the results are not similar in patients with DR. The macular thickness was found to be significantly increased post-operatively in SICS as compared to phacoemulsification, making phacoemulsification the better alternative in patients with pre-existing DR (Soni et al.,2020).

Early phacoemulsification in patients with DR has contributed to improved visual outcomes. This approach also facilitates early identification and adequate treatment of DR and its sequelae. In addition, if surgery is done before the lens opacifies due to cataract, the detection of retinal thickening may be facilitated, hence increasing the visual outcome (Kiziltoprak et al.,2019).

It is also important to reduce the time and complexity of the surgery since they are the main risk factors for the progression of retinopathy. Moreover, photic retinopathy especially during cataract surgeries of longer duration was also more prevalent in diabetic patients than non-diabetics (Kiziltoprak et al.,2019). Carefully performed cataract surgery in diabetic patients yields optimal results.

VEGF is an endothelial cell mitogen that enhances vascular permeability, causes collateral vessel formation, and increases microvascular permeability (Aiello et al., 1994). VEGF levels have been reported to be significantly correlated with the severity of DR (Funatsu et al., 2001). In eyes with DR, the intraocular level of VEGF and other inflammatory cytokines increases further after cataract surgery (Dong et al., 2015). Patel et al.(2006) found increased levels of VEGF 165 and other cytokines in aqueous samples of such patients. Surgical trauma and inflammation resulted in a rise in the concentration of angiogenic factors (Simo et al., 2006). These inflammatory mediators then cause the breakdown of the blood-retinal barrier and the blood-aqueous barrier, increasing vascular permeability and eventually macular thickness (Benitah et al., 2010). Following uneventful phacoemulsification, the incidence of ME ranges from 4%-11% (Kim et al., 2007) in non-diabetics; whereas it ranges from 20%-50% in patients with diabetes (Chung et al., 2002).

In a meta-analysis by Liu J. et al. (2015), uneventful phacoemulsification in patients with mild to moderate NPDR significantly increased the CMT than in diabetic patients without DR. In a study by Salehi A. et al. (2012), in patients with cataract and DR, administration of 1.25 mg of intravitreal bevacizumab at the time of cataract surgery was effective in preventing the progression of DR and diabetic maculopathy. It was shown that the rate of retinopathy progression was much higher in eyes that did not receive intravitreal bevacizumab than in those who received it.

On the other hand, El-Sobky HM et al. (2014) found that uncomplicated phacoemulsification did not cause acceleration of DR postoperatively. In addition, a benign course may be followed by any pre-existing ME and any progression would represent a natural progression rather than being a direct effect of surgery. It was also stated that posterior capsule rupture during cataract surgery in cases with DR led to a significant progression of DR, increased rates of ME, and foveal thickness. This could be explained by the breakdown of the blood-retinal barrier and the flow of inflammatory mediators from the aqueous to the posterior segment. Hence, during uncomplicated cases of phacoemulsification in DR, the adjuvant anti-VEGF injection doesn't play a significant role.

As in our study, all 32 eyes with cataract and NPDR underwent successful uneventful phacoemulsification without anti-VEGF injection. Similar to the results by El-Sobsy et al, our study gave favourable outcomes without any documented ME or significant increase in macular thickness in uncomplicated cases.

Due to the lack of bigger sample size studies and consensus guidelines in managing cataract in DR, it remains a matter of debate among surgeons to inject anti-VEGF during surgery. Hence, one has to weigh the benefits with possible adverse effects in individual cases and proceed accordingly.

CONCLUSION

Adjunctive anti-VEGF injection during phacoemulsification in eyes with treatment naïve diabetic retinopathy may be omitted. A significant increase in macular thickness requiring intravitreal anti-VEGF is not usually

seen if phacoemulsification is uneventful. Proper timely postoperative follow-up is a must to monitor the development of any complications. Hence, under proper glycaemic control, one can proceed safely with phacoemulsification rather than waiting for the availability of anti-VEGF agents or for retinopathy to resolve. This will provide better visual acuity to the patient and also proper monitoring and management of retinopathy.

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