



Comparison of the Effects of Phacoemulsification and Dexamethasone Implantation in the Same Session with Other Phakic Conditions

Yucel Ozturk,¹ Umit Calli,² Bengi Gungor,¹ Esra Turkseven Kumral,¹ Sevcan Yildiz Balci,¹
 Suleyman Kugu,¹ Nursal Melda Yenerel¹

¹Department of Ophthalmology, University of Health Sciences Haydarpaşa Numune Training and Research Hospital, İstanbul, Türkiye

²Department of Ophthalmology, University Health Sciences, Fatih Sultan Mehmet Training and Research Hospital, İstanbul, Türkiye

Abstract

Objectives: The objective of the study is to evaluate anatomical and functional results such as best corrected visual acuity (BCVA), central macular thickness (CMT), and intraocular pressure (IOP) in patients who received intravitreal dexamethasone (DEX) implant for diabetic macular edema (DME), and to compare the efficacy according to patients' lens status and concurrent phacoemulsification surgery.

Methods: A total of 70 eyes of 55 patients with DME who received intravitreal DEX implantation were included in this retrospective study. Patients who received intravitreal DEX implantation were divided into three groups phaco-DEX (group 1), pseudophakic (group 2), and phakic (group 3). The BCVA, CMT, and IOP changes were compared between the three groups.

Results: One month after the intravitreal DEX implant, BCVA improved in all three groups. ($p=0.001$, $p=0.01$, and $p=0.009$, respectively). There was a decrease in CMT at the end of 1st and 4th months in all three groups compared to the preoperative measurements ($p=0.005$, $p<0.001$, $p<0.001$ respectively). While IOP was increased in group 2 and group 3, no IOP increase was observed in group 1. ($p=0.41$, $p=0.01$, and $p=0.01$, respectively).

Conclusion: Combining intravitreal DEX implantation with phacoemulsification surgery seems to be an effective and reliable method in patients with DME accompanied by cataract. The IOP elevation in follow-up visits of phakic and pseudophakic patients after intravitreal DEX implantation was not observed in the Phaco-DEX group.

Keywords: Cataract, diabetic macular edema, intraocular pressure, intravitreal dexamethasone

Introduction

Diabetic Macular Edema (DME) is defined as retinal thickening at the center of the macula, which develops secondary to diabetic retinopathy (DR) and may be present at any stage

of the disease. The global prevalence of DME is 6.8% in DR patients aged 20–79 years (1).

Intravitreal administration of anti-inflammatory or anti-angiogenic agents has become the current standard treat-

How to cite this article: Ozturk Y, Calli U, Gungor B, Turkseven Kumral E, Yildiz Balci S, Kugu S, et al. Comparison of the Effects of Phacoemulsification and Dexamethasone Implantation in the Same Session with Other Phakic Conditions. *Beyoglu Eye J* 2023; 8(2): 81-90.

Address for correspondence: Yucel Ozturk, MD. Department of Ophthalmology, University of Health Sciences Haydarpaşa Numune Training and Research Hospital, İstanbul, Türkiye
Phone: +90 532 051 39 93 **E-mail:** yucellozturk@yahoo.com

Submitted Date: July 25, 2022 **Revised Date:** December 15, 2022 **Accepted Date:** January 10, 2023 **Available Online Date:** May 01, 2023

Beyoglu Eye Training and Research Hospital - Available online at www.beyoglueye.com

OPEN ACCESS This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



ment for the management of DME. The most common ocular side-effects associated with intravitreal steroids are increased intraocular pressure (IOP) and the development of cataracts, while the complications related to intravitreal injections include endophthalmitis, vitreous hemorrhage, and retinal detachment. To be able to reduce the risks and complications of intravitreal administration, intravitreal implants have been developed to provide continuous corticosteroid release for the treatment of DME (2-4).

An intravitreal implant of dexamethasone (DEX) (0.7 or 0.35 mg) (Ozurdex®; Allergan, Irvine, CA, USA) slowly releases steroids into the vitreous over a period of approximately 6 months. In 2014, the Food and Drug Administration approved intravitreal DEX implants for the treatment of DME, based on the results of the MEAD study (5).

Cataract is the leading cause of blindness worldwide. Previous studies have shown that the incidence of cataract formation is increased in patients with DM, and with cataract as one of the most frequent complications of DM, it is a major cause of visual impairment among the ocular complications of this disease, and up to 20% of all cataract procedures are performed for diabetic patients (6-8).

Optical coherence tomography (OCT) measurements of central macular thickness (CMT) have demonstrated an increase at 1 and 2 months after uncomplicated standard cataract surgery in diabetic patients. Even though the exact mechanism of macular edema after cataract surgery is not well defined, it is thought to be due to increased prostaglandin release and prostaglandin production secondary to free radical release in the postoperative period (9).

Both diabetes and phacoemulsification may result in increased macular thickness (9,10). Studies have reported significant visual improvements in patients who received intravitreal DEX implants combined with phacoemulsification compared to a control group, together with a significant decrease in CMT (11-13).

Many studies have examined the postoperative results of intravitreal DEX implantation performed in the same session as phacoemulsification for the treatment of DME (11-13). However, the effect of lens type on DEX implant outcomes and DME treatment is not clear as yet. There is no study in literature that has compared the effects of combined treatment with intravitreal DEX implant and phacoemulsification in phakic and pseudophakic patients. Therefore, the aim of this study was to evaluate the anatomic and functional results, such as best corrected visual acuity (BCVA), CMT, and IOP, in patients who received intravitreal DEX implant for DME and to compare the results according to the phakic status of the patients.

Methods

This retrospective, comparative, single-center case study included 70 eyes of 55 patients who were followed up for DME in the ophthalmology clinic of a tertiary-level university hospital and underwent intravitreal DEX implantation between 2016 and 2021. Approval for the study was granted by the Hospital Clinical Research Ethics Committee (2019/KK/51) and all procedures were in compliance with the principles of the Declaration of Helsinki.

The data were obtained from patient records. Eyes diagnosed with DR with clinically significant macular edema (CSME) in patients older than 18 years of age who did not respond to anti-vascular endothelial growth factor (VEGF) treatments (<20% decrease in macular thickness after 3 consecutive injections at 1-month intervals) and had 6-month follow-up data after intravitreal DEX implantation were included in the study. The presence of CSME was defined according to the Early Treatment Diabetic Retinopathy Study as retinal thickening at or within 500 microns or 1/3 disc diameter of the center of the macula, hard exudates at or within 500 microns of the center of the macula with adjacent retinal thickening, retinal thickening greater than 1 disc diameter in size which is within 1 disc diameter from the center of the macula (14). DME was characterized by sponge-like retinal swelling of the macula with low intraretinal reflectance.

The patients were divided into 3 groups patients with cataracts and DME who underwent both phacoemulsification and intravitreal DEX implantation in the same session (Group 1), pseudophakic patients with DME (Group 2), and phakic DME patients without lens opacification (Group 3). All eyes with cataracts in Group 1 were classified according to the Lens Opacities Classification System III (LOCS III) (15). Patients with N3-5 nuclear cataract, C4-5 cortical cataract, and P5 posterior subcapsular cataract required surgery at the time of intravitreal treatment, and therefore underwent a combined operation in a single session.

Eyes were excluded from the study if any complication developed during cataract surgery in Group 1, or if there was a history of complicated cataract surgery or neodymium-doped yttrium aluminum garnet laser capsulotomy and a follow-up period of less than 6 months after phacoemulsification in Group 2. Patients in all groups were also excluded if they had previously received intravitreal DEX implant or intravitreal triamcinolone acetonide treatment, had a history of vitreoretinal surgery or laser treatment within the past year, had any additional ocular pathologies such as vitreous hemorrhage, history of uveitis, glaucoma or ocular hypertension, or had incomplete follow-up data.

All patients included in the study underwent a complete ophthalmic evaluation, including BCVA evaluation, slit lamp biomicroscopic examination, indirect fundus ophthalmoscopy, and IOP measurement using Goldmann applanation tonometry. A Spectralis SD-OCT device (Spectralis; Heidelberg Engineering, Heidelberg, Germany) was used for OCT imaging. Acquisitions were carried out in raster scan mode to generate two-dimensional maps of the retina. The presence of DME was determined and the measured CMT values were recorded. For patients in all the groups, a record was made of the number of previous intravitreal injection treatments received.

Patients in Group 1 underwent standard phacoemulsification surgery, which was performed with a clear corneal incision under sterile conditions after preoperative pupil dilation with 1% tropicamide, and the intraocular lens (IOL) was placed in the capsular bag. An intravitreal 0.7 mg DEX implant (Ozurdex®; Allergan Inc., Irvine, CA, USA) was administered to the patients 3.5 millimeters away from the limbus using the product's injection applicator at the end of the surgery. Postoperatively, all the patients in Group 1 used topical moxifloxacin 0.5% and DEX 0.1% drops for 15 days. In Group 2 and Group 3, a 0.7 mg DEX implant was injected intravitreally through the pars plana with the product's applicator in the operating room under sterile conditions. Topical moxifloxacin 0.5% was applied after the injection.

The BCVA, IOP, and macular OCT values were recorded at 1 month and 4 months postoperatively for all the patients in all the groups. Topical anti-glaucomatous agents were started in patients with IOP of ≥ 22 mmHg measured at any follow-up visit. The patients were followed up for 6 months.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn. 22.0 software (IBM SPSS Statistics for Windows, Version 22.0. Published 2014. IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to evaluate the normal distribution of continuous variables. Parametric or non-parametric tests were applied according to the distribution of the data. Descriptive statistics were performed with numerical variables expressed as mean or median values, and categorical variables as number (n) and percentage (%). The CMT, BCVA, and IOP values of the patients at baseline and the 1st and 4th months were compared using the Paired Samples t-test or the Wilcoxon Signed Rank test. The differences between the groups were compared using the ANOVA test or Kruskal-Wallis test and pairwise comparison (Bonferroni) was made. The Friedman test was applied to compare data between groups due to the repeated data obtained from the same patients in multiple different measurements. A value of $p < 0.05$ was accepted as statistically significant.

Results

The evaluation was made of 70 eyes of 55 diabetic patients, comprising 17 eyes of 15 patients (8 males and 7 females) in Group 1 (Phaco-Dex), 29 eyes of 22 patients (14 males and 8 females) in Group 2 (Pseudophakic), and 24 eyes of 19 patients (10 males and 9 females) in Group 3 (Phakic). There was no difference between the groups in terms of gender ratio ($p=0.79$). The mean age was 62.9 ± 3.3 (55–71), with no statistically significant difference determined between the groups ($p=0.46$).

The number of anti-VEGF injections the patients received before intravitreal DEX was 5.7 ± 1.7 (4–10) in Group 1, 6 ± 1.5 (4–10) in Group 2, and 5.6 ± 1.1 (4–9) in Group 3 ($p=0.13$).

As shown in Table 1, 1 month after the intravitreal DEX implant, BCVA increased in all three groups. At 4 months after the intravitreal DEX implant, there was a significant improvement in vision in Groups 1 and 3 compared to the preoperative BCVA, whereas no significant difference was seen in Group 2 compared to the baseline measurements.

At the end of 1st and 4th months, CMT was decreased in all three groups compared to the preoperative measurements (Table 1). The CMT values showed a significant increase in the 4th month in Groups 2 and 3 compared to the CMT measured in the 1st month. No statistically significant difference in CMT was determined between the 1st and 4th months in Group 1.

At the follow-up visits, the elevation of IOP was observed in Group 2 and Group 3, and no IOP elevation was seen in Group 1 in the 1st and 4th months.

The repeated measures of BCVA, CMT, and IOP were seen to be statistically different over time (Table 2). A significant difference was determined between Groups 1 and 2 in respect of the BCVA values at the 4th month compared to the baseline measurements. Similarly, measurement of the CMT values showed a significant difference between Group 1 and Group 3 in the 1st month, and between Group 2 and Group 3 in the 4th month compared to the baseline CMT measurements. There was no difference in IOP measurements between the groups.

The comparisons of the 3 groups are shown in Table 3. At the end of the 4th month, the change in vision was significantly different between Group 1 and Group 2. The change in CMT was observed to be different between Group 1 and Group 3 at 1 month, and a statistically significant difference was determined between Group 2 and Group 3 in the 4th month. The comparisons of IOP showed a significant increase in Groups 2 and 3 compared to Group 1.

Table 1. Comparison of BCVA, CMT and IOP measurements according to time within the groups

Group	Mean \pm SD	Min	Max	Median	p* Baseline-1 st month	p*Baseline-4 th month	p* 1 st month-4 th month
BCVA (logMAR)							
1							
Baseline	0.99 \pm 0.48	0.40	2.00	0.69	0.001*	<0.001*	0.88
1 st month	0.58 \pm 0.30	0.22	1.00	0.39			
4 th month	0.52 \pm 0.23	0.22	1.00	0.52			
2							
Baseline	0.86 \pm 0.48	0.15	2.00	0.69	0.01*	0.82	0.01*
1 st month	0.73 \pm 0.48	0.15	2.00	0.69			
4 th month	0.85 \pm 0.52	0.15	2.00	0.69			
3							
Baseline	1.30 \pm 0.51	0.3	2.00	1.3	0.009*	0.03*	0.06
1 st month	1.04 \pm 0.58	0.4	2.00	0.52			
4 th month	1.14 \pm 0.56	0.4	2.00	1.0			
CMT (μ m)							
1							
Baseline	443 \pm 155	280	680	391	0.005*	0.006*	0.14
1 st month	315 \pm 59	237	405	336			
4 th month	333 \pm 55	251	431	332			
2							
Baseline	511 \pm 129	335	891	500	<0.001*	0.004*	<0.001*
1 st month	281 \pm 68	170	495	268			
4 th month	405 \pm 152	212	798	418			
3							
Baseline	598 \pm 191	340	1099	615	<0.001*	<0.001*	0.02*
1 st month	309 \pm 115	177	523	277			
4 th month	442 \pm 179	180	722	352			
IOP (mmHg)							
1							
Baseline	14 \pm 2.2	10	19	14	0.41	0.63	0.69
1 st month	14.4 \pm 2.8	9	18	14			
4 th month	14.3 \pm 1.8	10	17	15			
2							
Baseline	15 \pm 2.7	11	18	15	0.01*	0.11	0.09
1 st month	16.7 \pm 3.7	9	22	16			
4 th month	15.7 \pm 2.7	10	18	15			
3							
Baseline	15.7 \pm 2.4	11	21	15	0.01*	<0.001*	0.86
1 st month	18 \pm 2.8	13	24	20			
4 th month	17.9 \pm 3	14	24	18			

Paired t test, Wilcoxon signed ranks test; p* < 0.05, BCVA: Best-corrected visual acuity (logMAR); CMT: Central macular thickness; IOP: Intraocular pressure (mm Hg).

Table 2. Comparison of BCVA, CMT and IOP measurements according to time between the groups

	Baseline	1 st month	4 th month	p* Baseline-1 st month	p* Baseline-4 th month	p* 1 st month-4 th month
BCVA (logMAR)						
Group 1	0.99±0.48	0.58±0.30	0.52±0.23	0.001*	<0.001*	0.88
Group 2	0.86±0.48	0.73±0.48	0.85±0.52	0.01*	0.82	0.01*
Group 3	1.30±0.51	1.04±0.58	1.14±0.56	0.009*	0.03*	0.06
CMT (µm)						
Group 1	443±155	315±59	333±55	0.005*	0.006*	0.14
Group 2	511±129	281±68	405±152	<0.001*	0.004*	<0.001*
Group 3	598±191	309±115	442±179	<0.001*	<0.001*	0.02*
IOP (mmHg)						
Group 1	14±2.2	14.4±2.8	14.3±1.8	0.41	0.63	0.69
Group 2	15±2.7	16.7±3.7	15.7±2.7	0.01*	0.11	0.09
Group 3	15.7±2.4	18±2.8	17.9±3	0.01*	<0.001*	0.86

Friedman test, P* < 0.05, BCVA: Best-corrected visual acuity; CMT: Central macular thickness; IOP: Intraocular pressure.

Discussion

This study was conducted to evaluate the efficacy of the intravitreal DEX implant (Ozurdex®) in patients with DME according to the lens status of the patients, in addition to the effect of combining the treatment with concurrently performed phacoemulsification. In particular, the BCVA, CMT, and IOP values were evaluated at follow-up visits and the measurements were compared between the groups. The results showed that the intravitreal DEX implant resulted in improved BCVA and decreased CMT values. Furthermore, while IOP elevations were observed in the phakic and pseudophakic groups during follow-up visits, the absence of any increase in IOP in the Phaco-DEX group is one of the interesting findings of this study.

The most common cause of vision loss associated with DR is DME, which is estimated to affect 20% of patients with DR. DME is characterized by the thickening of the macular region caused by the movement of fluid across the blood-retinal barrier (BRB) due to the breakdown of the BRB. Inflammation has an important role in the pathogenesis of DME as the breakdown of the BRB involves the expression of inflammatory factors including VEGF, intercellular adhesion molecule-1, interleukin-6 and monocyte chemoattractant protein-1. Leukostasis and changes in endothelial tight junction proteins are responsible for this event. Treatment of DME involves laser photocoagulation and intravitreal anti-VEGF agents such as bevacizumab, ranibizumab, and aflibercept. Intravitreal corticosteroids may also be useful in the treatment of DME as they block the production of VEGF and other inflammatory mediators, inhibit leukostasis, and enhance the barrier function of tight junctions in vascular en-

dothelium. Ozurdex®, a sustained-release intravitreal DEX implant, is used for the treatment of DME (16-18).

The mechanism of macular edema occurring after cataract surgery is defined as the increased production of prostaglandins secondary to free radical release in the postoperative period due to mechanical traction caused by vitreoretinal adhesions and excessive light exposure on the retina. Biro et al. suggested that an increase in CMT could be measured with OCT in the 1st and 2nd months after uncomplicated standard cataract surgery in diabetic patients. Despite the current-day applications of modern small-incision cataract surgery, macular changes are still observed in the postoperative period in diabetic patients (14,19). Apart from post-surgical cystoid macular edema due to increased permeability in retinal capillaries caused by postoperative inflammatory reactions (Irvine-Gass syndrome), cataract surgery may also result in the progression of pre-existing DR and DME, as well as the development of new-onset retinopathy in diabetic eyes without a previous diagnosis of DR. Intravitreal corticosteroids have been found to be effective on both the diabetic and inflammatory pathways of postoperative macular edema (13,20).

Both diabetes and phacoemulsification may result in increased CMT. In the current study, the efficacy of intravitreal DEX implants was investigated in patients who had both of the risk factors. The results were compared between the groups that received intravitreal DEX implant according to whether the patients had previous cataract surgery, or underwent surgery at the time of intravitreal treatment. There are several studies in the current literature which have compared the efficacy of intravitreal DEX in phakic and

Table 3. Alterations in BCVA, CMT and IOP during follow-ups in groups and pairwise groups

Group	Mean±SD	Min.	Max.	Median	P*	P* Group 1-2	P* Group 1-3	P* Group 2-3
BCVA (logMAR)								
Baseline								
1	0.99±0.48	0.40	2.00	0.69	0.005*	1.0	0.14	0.004*
2	0.86±0.48	0.86±0.48	0.15	2.00	0.69			
3	1.30±0.51	0.3	2.00	1.3				
1st month								
1	0.58±0.30	0.22	1.00	0.39	0.01*	1.0	0.01*	0.07
2	0.73±0.48	0.15	2.00	0.69				
3	1.04±0.58	0.4	2.00	0.52				
4th month								
1	0.52±0.23	0.52±0.23	0.22	1.00	0.13	0.13	0.01*	0.12
2	0.85±0.52	0.15	2.00	0.69				
3	1.14±0.56	0.4	2.00	1.0				
Difference between 1st month and baseline								
1	0.26±0.40	-0.6	1.08	0.3	0.37	0.81	1.0	0.64
2	0.13±0.26	-0.32	1.00	0				
3	0.25±0.44	-0.3	1.48	0				
Difference between 4th month and baseline								
1	0.37±0.28	-1.0	0	-0.30	0.002*	0.001*	0.11	0.23
2	0.01±0.27	-0.78	0.70	0				
3	0.16±0.32	-0.70	0.30	0				
Difference between 4th month and 1st month								
1	0.00±0.12	0	0.12	0	0.21	0.25	0.57	1.0
2	0.10±0.21	-0.22	0.70	0				
3	0.08±0.19	0	0.78	0				
CMT (µm)								
Baseline								
1	443±155	280	680	391	0.01*	0.51	0.009*	0.17
2	511±129	335	891	500				
3	598±191	340	1099	615				
1st month								
1	315±59	237	405	336	0.35	0.59	1.0	0.79
2	281±68	170	495	268				
3	309±115	177	523	277				
4th month								
1	333±55	251	431	332	0.09	0.36	0.09	1.0
2	405±152	212	798	418				
3	1.14±0.56	180	722	352				
Difference between 1st month and baseline								
1	127±163	-275	-10	-43	0.006*	0.62	0.006*	0.07
2	204±185	-552	-5	-215				
3	328±230	-845	-25	-266				

Table 3. CONT.

Group	Mean±SD	Min.	Max.	Median	P*	P* Group 1-2	P* Group 1-3	P* Group 2-3
Difference between 4th month and baseline								
1	128±164	-249	18	-36	0.02*	1.0	0.11	0.02*
2	112±206	-400	156	-72				
3	267±231	-449	171	-169				
Difference between 4th month and 1st month								
1	1.1±100	-27	63	11	0.23	0.27	0.81	1.0
2	91±212	-57	459	148				
3	61±174	-39	409	85				
IOP (mmHg)								
Baseline								
1	14±2.2	10	19	14	0.13	0.6	0.14	1.0
2	15±2.7	11	18	15				
3	15.7±2.4	11	21	15				
1st month								
1	14.4±2.8	9	18	14	0.07	0.09	0.005*	0.48
2	16.7±3.7	9	22	16				
3	18±2.8	13	24	20				
4th month								
1	14.3±1.8	10	17	15	0.01*	0.42	0.002*	0.02*
2	15.7±2.7	10	18	15				
3	17.9±3	14	24	18				
Difference between 1st month and baseline								
1	0.35±1.7	-2	2	0	0.13	0.41	0.14	1.0
2	1.6±3.3	-3	9	2				
3	2.2±2.9	-3	9	3				
Difference between 4th month and baseline								
1	0.53±3.3	-3	3	0	0.74	1.0	1.0	1.0
2	0.14±3.8	-4	6	1				
3	0.58±6	-3	6	3				
Difference between 4th month and 1st month								
1	0.88±4.7	-2	5	0	0.87	1.0	1.0	1.0
2	1.55±4.1	-9	8	0				
3	1.63±5.7	-5	5	0				

ANOVA test, Kruskal-Wallis test; p* $<$ 0.05, BCVA: Best-corrected visual acuity; CMT: Central macular thickness; IOP: Intraocular pressure.

pseudophakic patients, as well as studies which have investigated DME progression in patients who have undergone phacoemulsification and intravitreal DEX implant in the same session compared to control groups. However, to the best of our knowledge, no study in literature has compared the combined application of Phaco-DEX to phakic and pseudophakic patients receiving intravitreal DEX implant.

Agarwal et al. reported a significant increase in BCVA in patients who underwent phacoemulsification and intravitreal DEX implant compared to a control group (phacoemulsification only). There was also reported to be a significant reduction in the CMT of the patient group, while the control group showed no decrease in CMT (11). Furino et al. demonstrated a significant reduction in central retinal thick-

ness and increase in visual acuity in a study of 16 patients with a follow-up period of 3 months, and it was suggested that combined phacoemulsification and intravitreal DEX implantation had an effect on morphological and functional results for at least 3 months after the operation (7). Sze et al. reported decreased macular thickness and increased vision with phacoemulsification and intravitreal DEX injections in a study conducted on 32 eyes of patients with macular edema resulting from diabetes or retinal vein occlusion (12). Panozzo et al. concluded that intravitreal DEX implant prevented the deterioration caused by phacoemulsification and this effect lasted for at least 3 months (13).

In the results of the current study, consistent with the literature, in the Phaco-DEX group a significant reduction was observed in CMT and improvement in vision in the 1st and 4th postoperative months compared to the baseline measurements. However, no statistically significant difference was determined between the measurements conducted in the 1st and 4th postoperative months.

In contrast, pseudophakic patients who received intravitreal DEX implant showed an improvement in BCVA and a decrease in CMT in the 1st month. However, in the 4th month, CMT showed a significant increase compared to the 1st month, despite the values remaining lower than baseline measurements, and no significant difference in BCVA was seen compared to baseline, showing that the temporary vision improvement was not sustained as the CMT increased and ultimately the vision improvement in patients with relatively lower CMT was not significantly different from the baseline value.

The phakic patients who received intravitreal DEX implant without cataract surgery, the CMT decreased in the 1st month then showed an increase in the 4th month, while remaining lower than baseline, as observed in pseudophakic patients. However, the increase in BCVA in the 1st month remained significant in the 4th month compared to baseline, despite the increase in CMT. These results suggest that the sustained vision improvement despite increased CMT in the phakic group was due to the less significant increase in CMT in the 1st and 4th months compared to the pseudophakic group. The increased aqueous outflow in pseudophakic patients may contribute to the earlier clearance of DEX from the vitreous, thereby resulting in a shorter period of efficacy. Nevertheless, no significant increase was observed in CMT between the 1st and 4th months in the Phaco-DEX group despite the increased outflow resulting from cataract surgery.

In addition to the anatomic and functional benefits, the most common adverse effects associated with intravitreal DEX implants are elevation in IOP and cataract development (5). Steroid-induced IOP increase is believed to be due to the changes in the trabecular meshworkTM and Sch-

lemm's canal, such as increased cell size and extracellular matrix, altered cell junctions, and reorganization of the TM cytoskeleton, thereby affecting the aqueous outflow resistance (21). Kaldirim et al. published a series of 79 patients in which the effect of an intravitreal DEX implant on DME was compared in pseudophakic and phakic patients (22). While an increase in vision was reported in both groups, it was also seen that the pseudophakic group experienced significantly earlier and higher levels of increase in IOP compared to the phakic group. It was suggested that in pseudophakic eyes, facilitated aqueous flow through the anterior chamber results in the earlier effects of DEX particles on the TM structure (22). In the current study, an early increase in IOP was observed in both the phakic and the pseudophakic groups, although the patients in the Phaco-DEX group showed no IOP elevation in the follow-up visits. This may be due to the IOP-lowering effect of phacoemulsification surgery (8,12,14,19). The Ocular Hypertension Treatment Study concluded that phacoemulsification cataract surgery and IOL implantation lowers postoperative IOP by 16.5% and decreased levels are sustained for at least a year (23). Shingleton et al. studied the effects of phacoemulsification in patients with suspected glaucoma and without glaucoma and showed that IOP decreased by mean 1.5 mmHg in all groups including patients without ocular hypertension or glaucoma (24). Combining intravitreal DEX implantation with phacoemulsification surgery may be beneficial for preventing IOP elevation. In a post-mortem study of human eyes, Van Buskirk demonstrated that lens depression and mechanical tension on the zonules are associated with a decrease in outflow resistance. The increase in mechanical tension on the zonules and iridocorneal angle induced by IOL implantation may provide increased facility of outflow by widening the spaces in the trabecular meshwork, and therefore prevent the IOP-increasing effects of DEX when combined with cataract surgery (23,25).

Several studies have reported IOP elevation after DEX implantation. While Panozzo et al. and Furino et al. reported increased IOP in Phaco-DEX patients, Agarwal et al. and Sze et al. did not observe an increase in IOP (7,11-13). In the current study, no increase in IOP that would require medication in the postoperative follow-up period was observed in any of the patients.

This study had several limitations, primarily the retrospective design and the range of data presented was relatively small. Moreover, the duration of DM, use of insulin or oral antidiabetic drugs, blood glucose regulation, HbA1C levels, or involvement of other organs with tissue damage related to DM complications were not taken into consideration.

Conclusion

Combining intravitreal DEX implants with phacoemulsification surgery seems to be an effective and reliable method in patients with DME accompanied by cataract. The feared increase in IOP in patients who have received intravitreal DEX implant was not observed in the Phaco-Dex patients compared to the phakic and pseudophakic patients who received only intravitreal DEX implant. Therefore, it can be suggested that combining the intravitreal DEX implantation with phacoemulsification surgery, will enable benefits to be obtained from the IOP-lowering effects of cataract surgery in patients who require intravitreal DEX while utilizing the preventive effects of DEX on postoperative inflammatory reactions and deterioration of pre-existing DR and DME with long-term efficacy. Although there are relevant studies in the literature, there is a need for further studies with larger populations to accurately evaluate the effectiveness and safety of this treatment.

Disclosures

Ethics Committee Approval: Approval for the study was granted by the Hospital Clinical Research Ethics Committee (2019/KK/51) and all procedures were in compliance with the principles of the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – Y.O.; Design – Y.O., S.K.; Supervision – S.K., N.M.Y.; Resource – Y.O., E.T.K., N.M.Y.; Materials – Y.O.; Data collection and/or processing – Y.O.; Analysis and/or interpretation – U.C., Y.O.; Literature search – C.B.G.; Writing – Y.O., S.B.; Critical review – N.M.Y.

References

1. He Y, Ren XJ, Hu BJ, Lam WC, Li XR. A meta-analysis of the effect of a dexamethasone intravitreal implant versus intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema. *BMC Ophthalmol* 2018;18:121. [CrossRef]
2. Lattanzio R, Cicinelli MV, Bandello F. Intravitreal steroids in diabetic macular edema. *Dev Ophthalmol* 2017;60:78–90. [CrossRef]
3. Tabakci BN, Unlu N. Corticosteroid treatment in diabetic macular edema. *Turk J Ophthalmol* 2017;47:156–60. [CrossRef]
4. Yuen YS, Tan GS, Gan NY, Too IH, Mothe RK, Basa P, et al. Real-world evidence in the management of diabetic macular edema with intravitreal anti-VEGFs in Asia: A systematic literature review. *Clin Ophthalmol* 2022;16:3503–26. [CrossRef]
5. Boyer DS, Yoon YH, Belfort R Jr., Bandello F, Maturi RK, Augustin AJ, et al. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. *Ophthalmology* 2014;121:1904–14. [CrossRef]
6. Li L, Wan XH, Zhao GH. Meta-analysis of the risk of cataract in Type 2 diabetes. *BMC Ophthalmol* 2014;14:94. [CrossRef]
7. Furino C, Boscia F, Niro A, Giampiloli E, Grassi MO, Ricci GD, et al. Combined phacoemulsification and intravitreal dexamethasone implant (Ozurdex®) in diabetic patients with co-existing cataract and diabetic macular edema. *J Ophthalmol* 2017;2017:4896036. [CrossRef]
8. Martinez MB, Moyano DB, Gonzalez-Lezcano RA. Phacoemulsification: Proposals for improvement in its application. *Healthcare (Basel)* 2021;9:1603. [CrossRef]
9. Biro Z, Balla Z, Kovacs B. Change of foveal and perifoveal thickness measured by OCT after phacoemulsification and IOL implantation. *Eye (Lond)* 2008;22:8–12. [CrossRef]
10. Chauhan MZ, Rather PA, Samarah SM, Elhusseiny AM, Sallam AB. Current and novel therapeutic approaches for treatment of diabetic macular edema. *Cells* 2022;11:1950. [CrossRef]
11. Agarwal A, Gupta V, Ram J, Gupta A. Dexamethasone intravitreal implant during phacoemulsification. *Ophthalmology* 2013;120:211, 211.e1–5. [CrossRef]
12. Sze AM, Luk FO, Yip TP, Lee GK, Chan CK. Use of intravitreal dexamethasone implant in patients with cataract and macular edema undergoing phacoemulsification. *Eur J Ophthalmol* 2015;25:168–72. [CrossRef]
13. Panozzo GA, Gusson E, Panozzo G, Mura GD. Dexamethasone intravitreal implant at the time of cataract surgery in eyes with diabetic macular edema. *Eur J Ophthalmol* 2017;27:433–7.
14. Gangnon RE, Davis MD, Hubbard LD, Aiello LM, Chew EY, Ferris FL 3rd, et al. A severity scale for diabetic macular edema developed from ETDRS data. *Invest Ophthalmol Vis Sci* 2008;49:5041–7. [CrossRef]
15. Chylack LT Jr., Wolfe JK, Singer DM, Leske MC, Bullimore MA, Bailey IL, et al. The lens opacities classification system III. The longitudinal study of cataract study group. *Arch Ophthalmol* 1993;111:831–6. [CrossRef]
16. Haller JA, Bandello F, Belfort R Jr., Blumenkranz MS, Gillies M, Heier J, et al. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. *Ophthalmology* 2010;117:1134–46.e3.
17. Diabetic Retinopathy Clinical Research Network, Wells JA, Glassman AR, Ayala AR, Jampol LM, Aiello LP, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. *N Engl J Med* 2015;372:1193–203. [CrossRef]
18. Teja S, Sawatzky L, Wiens T, Maberley D, Ma P. Ozurdex for refractory macular edema secondary to diabetes, vein occlusion, uveitis and pseudophakia. *Can J Ophthalmol* 2019;54:540–7. [CrossRef]
19. Yavuz L, Kugu S, Yilmaz I, Ozturk Y, Ozerturk Y. Results of phacoemulsification surgery in diabetic and non-diabetic patient groups. *J Kartal Train Res Hosp* 2013;24:103–7. [CrossRef]
20. Diabetic Retinopathy Clinical Research Network Authors/ Writing Committee, Baker CW, Almuthtar T, Bressler NM, Glassman AR, Grover S, et al. Macular edema after cataract surgery in eyes without preoperative central-involved diabetic macular edema. *JAMA Ophthalmol* 2013;131:870–9. [CrossRef]

21. Clark AF, Brotchie D, Read AT, Hellberg P, English-Wright S, Pang IH et al. Dexamethasone alters F-actin architecture and promotes cross-linked actin network formation in human trabecular meshwork tissue. *Cell Motil Cytoskeleton* 2005;60:83–95.
22. Kaldirim H, Savur F, Kirgiz A, Atalay K. Comparison of anatomical and functional outcomes of intravitreal dexamethasone implant between phakic and pseudophakic eyes with diabetic macular edema. *Korean J Ophthalmol* 2020;34:383–91.
23. Mansberger SL, Gordon MO, Jampel H, Bhorade A, Brandt JD, Wilson B, et al. Reduction in intraocular pressure after cataract extraction: The Ocular Hypertension Treatment Study. *Ophthalmology* 2012;119:1826–31.
24. Shingleton BJ, Pasternack JJ, Hung JW, O'Donoghue MW. Three and five year changes in intraocular pressures after clear corneal phacoemulsification in open angle glaucoma patients, glaucoma suspects, and normal patients. *J Glaucoma* 2006;15:494–8.
25. Van Buskirk EM. Changes in the facility of aqueous outflow induced by lens depression and intraocular pressure in excised human eyes. *Am J Ophthalmol* 1976;82:736–40.