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ORIGINAL RESEARCH

Impact of Different Clinical Baseline Characteristics on Intravitreal Dexamethasone Implant Ozurdex® Outcomes

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Purpose: To determine the impact of different baseline clinical characteristics on the improvement in best corrected visual acuity (BCVA) in patients with diabetic macular edema (DME) who underwent the intravitreal dexamethasone implant (DEX) Ozurdex®.

Methods: This was a single center retrospective study conducted on patients with DME, either naïve or previously treated, who were treated with one or more DEX and had a follow-up of at least 6 months. The main outcome measure was the proportion of DEX achieving an improvement ≥15 letters in BCVA.

Results: The study analyzed 192 DEX implants administered to 97 eyes (65 patients). Among the 192 DEX analyzed, 57 (29.7%) implants achieved a BCVA improvement ≥15 letters (ETDRS) from baseline, with a mean time for achieving such improvement of 89.2 (39.7) days. Eyes who received an additional DEX and those with a duration of DME < 6 months had a greater probability of achieving a BCVA improvement ≥15 letters (odds-ratio: 2.55, $p = 0.0028$ and odds-ratio: 1.93, $p = 0.0434$). The mean (standard deviation) change in BCVA from baseline was 7.5 (14.5) letters, $p < 0.0001$. The mean change in central macular thickness (CMT) from baseline was −128.0 (151.0) µm, $p < 0.0001$. The mean number of DEX implanted was 1.9 (0.8). Four (2.1%) DEX experienced an intraocular pressure increased ≥10 mm Hg; all the cases were successfully managed with topical antiglaucoma medication.

Conclusion: The results of this study confirmed previous evidence suggesting that DEX is effective for improving BCVA and CMT in patients with DME.

Keywords: diabetic macular edema, dexamethasone intravitreal implant, Ozurdex, best corrected visual acuity, central macular thickness

Introduction

Among the different currently available options for treating diabetic macular edema (DME), intravitreal corticosteroids and vascular endothelial growth factor inhibitors (anti-VEGF) have emerged as first-line treatment for this pathology.[1]

DME presents complex and multifactorial pathogenic mechanisms, with different factors including chronic hyperglycemia, hypercholesterolemia, free oxygen radicals, advanced glycation end-products and protein kinase C involved in its pathophysiologic process.[2]

Because inflammation has been identified as an important pathophysiological mechanism in DME, corticosteroids have taken an active role in the treatment of DME.[3] Corticosteroids inhibit many of the processes involved in the pathophysiology of the DME, through anti-inflammatory properties[4] and VEGF inhibition.[5]

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Over the past several years, slow-release intravitreal corticosteroid implants, including dexamethasone posterior segment delivery system (Ozurdex, Allergan, Irvine, CA, United States),[6] and fluocinolone (Iluvien, Alimera Sciences Limited, Aldershot, UK)[7] have been commercially available.

According to the European Society of Retina Specialists (EURETINA) Guidelines, in DME patients, dexamethasone should be used first, while fluocinolone is recommended in patients with chronic DME who did not respond to other treatments.[1]

Many different studies have demonstrated that the intravitreal dexamethasone implant (DEX) Ozurdex® significantly improved the functional (visual acuity) and anatomic (central macular thickness) outcomes in patients with DME.[8–16] However, the impact of different baseline clinical characteristics on DEX outcomes has not been fully elucidated.

Because not all patients respond similarly to DME treatment, determining potential predictive factors is crucial for customizing treatment and optimizing clinical outcomes.

Different optical coherence tomography (OCT) biomarkers, including presence of submacular fluid, absence/number of hyperreflective foci, integrity of the inner segment-outer segment, outer nuclear layer, disorganization of the retinal inner layers, outer retinal layer, and presence of cysts have been identified as prognostic and predictive factors in patients with DME.[17–20]

The purpose of this study was to determine the impact of different baseline clinical characteristics on the improvement in best corrected visual acuity (BCVA) in patients with DME who underwent the DEX Ozurdex®.

Methods

Design

Single center retrospective study conducted on patients with diabetic macular edema, either naïve or previously treated, referred or recruited in a third-level hospital.

Study protocol was approved by the Institutional Review Board of the La Fe University Hospital with the number (2014/00373/EO) and the study was conducted in accordance with the rules of the Declaration of Helsinki. The board waived the need for informed consent for study participation, since it was a retrospective study.

The data was anonymized for preserving the confidentiality of patients and will only be used for purposes related to this research.

Patient Eligibility

Patients with DME, who were treated with one or more intravitreal dexamethasone implant and had a follow-up of at least 6 months.

Inclusion criteria included age ≥18 years; a diagnosis of type 1 or 2 diabetes; DME (naïve or previously treated) with central macular thickness (CMT) ≥300 µm, a BCVA of 20/200 (35 letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) charts) and had medical chart data available for at least 6 months after receiving the first DEX. Patients were excluded if they had macular edema due to any other condition; history of major ocular surgery, except non-complicated cataract surgery, within the previous 6 months or an intraocular pressure (IOP) ≥ IOP >21 mm Hg with one medication or any use of 2 or more medications. DME patients who received treatment with intravitreal triamcinolone ≤6 months before baseline or intravitreal bevacizumab, ranibizumab, or aflibercept ≤3 months before baseline were also excluded.

Cataract was assessed according to the lens Opacities Classification System.[21]

Study Variables

For each patient, data collected at the baseline visit included demographics; mean BCVA [letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) charts]; CMT; IOP; IOP lowering medications; duration of diabetes; duration of DME; HbA1c; previous treatment of DME; DME perfusion status and lens status.

Variables collected during the follow-up included proportion of implants with BCVA improvement ≥15 letters (ETDRS) from baseline; time to ≥15 letters (ETDRS) improvement from baseline; proportion of implants with BCVA improvement ≥10 letters (ETDRS) from baseline; time to ≥10 letters (ETDRS) improvement from baseline; mean change in BCVA from baseline; time to peak improvement in BCVA from baseline; mean change in CMT from baseline; time to peak improvement in CMT from baseline; proportion of implants with BCVA reduction ≥15 letters (ETDRS) from baseline; time to ≥15 letters (ETDRS) reduction from baseline; proportion of implants with BCVA reduction ≥10 letters (ETDRS) from baseline; time to ≥10 letters (ETDRS) reduction from baseline and number of implants.

DEX 0.7 mg was injected into the vitreous cavity using standard protocols.[9]

After the DEX implantation, retreatment was judged necessary at the scheduled follow-up visits if recurrence of DME and/or intraretinal (IRF)/subretinal (SRF) were present or if BCVA decreased due to recurrence of macular edema.

Retreatment criteria were based on a pro-re-nata treatment regime. There were two anatomic criteria and one functional criterion for retreatment. The anatomic criteria were a CMT increase of 50 µm in OCT measurements or the onset of new cysts as compared to the previous visit. The functional criterion was a BCVA loss ≥5 ETDRS letters due to DME and not secondary to other causes, such as cataract or optical changes.

Outcomes

The main outcome measure was the proportion of DEX achieving an improvement ≥15 letters in BCVA and risk factors significantly associated with BCVA improvement ≥15 letters.

Secondary outcome measures included the mean change in BCVA from baseline, mean change in CMT from baseline; risk factors significantly associated with BCVA improvement ≥10 letters; proportion of implants achieving a BCVA improvement ≥10 letters; time to ≥15 letters (ETDRS) improvement from baseline; time to ≥10 letters (ETDRS) improvement from baseline; time to peak improvement in BCVA from baseline; time to peak improvement in CMT from baseline; proportion of implants with BCVA reduction ≥15 letters (ETDRS) from baseline; time to ≥15 letters (ETDRS) reduction from baseline; proportion of implants with BCVA reduction ≥10 letters (ETDRS) from baseline; time to ≥10 letters (ETDRS) reduction from baseline; number of implants and adverse events.

Statistical Analysis

A standard statistical analysis was performed using SAS ® version 9.3 (SAS Institute, Cary North Carolina) and the statistical program MedCalc version 20.008 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2021).

Descriptive statistics number (percentage), mean [standard deviation (SD)], mean [95% confidence interval (95% CI)], mean [standard error (SE)] or median (95% CI) were used, as appropriate.

Comparisons between pre-intervention and post-intervention values were performed for BCVA and central macular thickness (CMT).

Normal distribution of continuous variables was evaluated by means D'Agostino-Pearson test.

As data were normally distributed, the two-way paired samples Student's *t*-test was used to compare means between pre-intervention and post-intervention values.

A logistic regression model was used to assess and test factors for their association with achieving an improvement in BCVA ≥ 15 letters and ≥10 letters.

For the logistic regression analysis, the study subjects were divided according to their lens status (phakic vs pseudophakic); DME perfusion status (non-ischemia vs ischemia); DME status (naïve vs previously treated); duration of DME (<6 months vs ≥6 months); HbA1c (≤8% vs >8%) and DEX implanted (first DEX vs subsequent ones).

A p value <0.05 was considered as statistically significant.

Results

The study analyzed 192 DEX implants administered to 97 eyes (65 patients). Their main demographic and clinical characteristics are shown in Table 1.

Mean age was 67.1±9.9 years and 32 (49.8%) patients were women. Mean HbA1c was 8.2%±1.1%. Sixty-seven (69.1%) eyes were naïve and 30 (30.9%) ones had undergone previous DME treatment.

Among the 192 DEX analyzed, 57 (29.7%) implants achieved a BCVA improvement ≥15 letters (ETDRS) from baseline, with a mean time for achieving such improvement of 89.2±39.7 days. Eighty-four (43.8%) implants achieved an improvement in BCVA ≥ 10 letters (ETDRS) from baseline and the mean time for achieving that improvement was 93.6±36.8 days.

On the negative side, as compared to baseline, 24 (12.5%) implants presented a reduction in BCVA ≥ 15 letters (ETDRS) and 31 (16.1%) ones a reduction in BCVA ≥ 10 letters.

The mean (SD) change in BCVA from baseline was 7.5±14.5 letters, $p < 0.0001$ (Figure 1).

The mean change in CMT from baseline was −128.0±151.0 µm, $p < 0.0001$ (Figure 2). The mean number of DEX implanted was 1.9±0.8.

Main clinical outcomes are presented in Table 2.

Baseline BCVA did not show no significant differences among the different comparisons, depending on lens status (Phakic vs Pseudophakic); perfusion status (without ischemia vs with ischemia); DME status (Naïve vs Previously treated); duration of DME (<6 months vs ≥6 months);

Table 1 Baseline Demographic and Clinical Characteristics of the Study Sample

Number	
Subjects	65
Eyes	97
Age, years	
Mean (SD)	67.1 (9.9)
Range	37 to 85
Sex, n (%)*	
Male	33 (50.8)
Female	32 (49.2)
BCVA, letters†	
Mean (SD)	64.7 (11.5)
CMT, µm	
Mean (SD)	458.0 (120.0)
IOP, mm Hg	
Mean (SD)	16.5 (2.9)
PUAM, n (%)	0 (0.0)
HbA1c, %*	
Mean (SD)	8.2 (1.1)
Duration of DM, years	
Mean (SD)	14.2 (9.5)
Duration of DME, months	
Mean (SD)	12.6 (16.8)
Previous treatment, n (%)**	
None	67 (69.1)
Focal/grid Laser	58 (59.8)
Anti-VEGF	34 (35.1)
IVC	0 (0.0)
DME perfusion status	
Ischemic	76 /78.4)
Non-ischemic	21 (21.6)
Lens status, n (%)	
Phakic	48 (49.5)
Pseudophakic	49 (50.5)

Notes: *Based on number of subjects. **Eyes could undergo multiple treatment types. †Letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) charts. **Abbreviations**: SD, standard deviation; BCVA, best corrected visual acuity; CMT, central macular thickness; IOP, intraocular pressure; PUAM, Patients using antiglaucoma medication; DM, Diabetes Mellitus; DME, diabetic macular edema; VEGF, vascular endothelial growth factor; IVC, intravitreal corticosteroids.

HbA1c levels (≤8% vs >8%); or DEX (First vs Subsequent) (Figure 3).

As compared to baseline, mean change in BCVA was +5.8±16.7 and 9.1±11.9 letters in phakic and pseudophakic eyes, respectively (mean difference −3.3 letters; 95% CI: −8.5 to 2.0 letters, p = 0.2232); +6.8±14.1 and 10.2±15.9 letters in eyes without and with macular ischemia, respectively (mean difference −3.4 letters; 95% CI: −9.8 to 2.9 letters, p = 0.2860); +8.5±15.2 and +5.3±12.5 letters in naïve and previously treated eyes, respectively (mean difference 3.2 letters; 95% CI: −2.5 to 8.9 letters, p = 0.2729); +8.9±13.7 and +5.7±15.4 in eyes with a DME duration <6 months and ≥6 months, respectively (mean difference 3.2 letters; 95% CI: −2.1 to 8.5 letters, p = 0.2283); +8.8±15.4 and 6.7±14.0 letters in patients with HbA1c ≤8% and >8%, respectively (mean difference 2.1 letters; 95% CI: −3.3 to 7.5 letters, p = 0.4519); and +5.4 ±13.0 and 6.1±15.8 letters with the First and subsequent DEX implants, respectively (mean difference −0.7 letters; 95% CI: −5.1 to 3.7 letters, p = 0.7618).

Regarding the logistic regression analysis, as compared with the first DEX, received an additional DEX was significantly associated with a greater probability of achieving a BCVA improvement ≥15 letters from baseline (Odds ratio: 2.55; 95% CI: 1.38 to 4.72; p = 0.0028). Additionally, eyes with a DME duration <6 months had a significant greater probability of achieving a BCVA improvement ≥15 letters from baseline (Odds ratio: 1.93; 95% CI: 1.02 to 3.67; p = 0.0434) (Table 3). However, lens status (phakic vs pseudophakic); DME perfusion status (non-ischemia vs ischemia); DME status (naïve vs previously treated); and HbA1c (≤8% vs >8%) were no significant predictors of achieving a BCVA improvement ≥15 letters from baseline (Table 3).

DME status (p = 0.0295); duration of DME (p = 0.0040); and received an additional DEX (p = 0.0002) were significantly associated with the probability of achieving a BCVA improvement ≥10 letters. Test factors and their association with achieving an improvement in BCVA ≥ 10 letters are shown in Table 4.

The proportion of DEX with a BCVA reduction ≥10 letters (22.3% vs 10.2%) and ≥15 letters (19.1% vs 6.1%) were significantly greater in the phakic than in the pseudophakic eyes, p = 0.0188 and p = 0.0054, respectively. Additionally, the DEX implanted in eyes with a duration of DME ≥ 6 months had a greater proportion of implants with a BCVA reduction ≥10 letters and ≥15 letters (25.9% and 20.0%, respectively) than those with a duration of DME < 6 months (8.7% and 6.8%, respectively), p = 0.0007 and 0.0037, respectively.

The time for achieving an improvement ≥15 letters in BCVA was significantly shorter in the naïve eyes than in the previously treated ones 76.9±32.0 vs 127±28.8 days, respectively, p < 0.0001. There was a 11% difference in

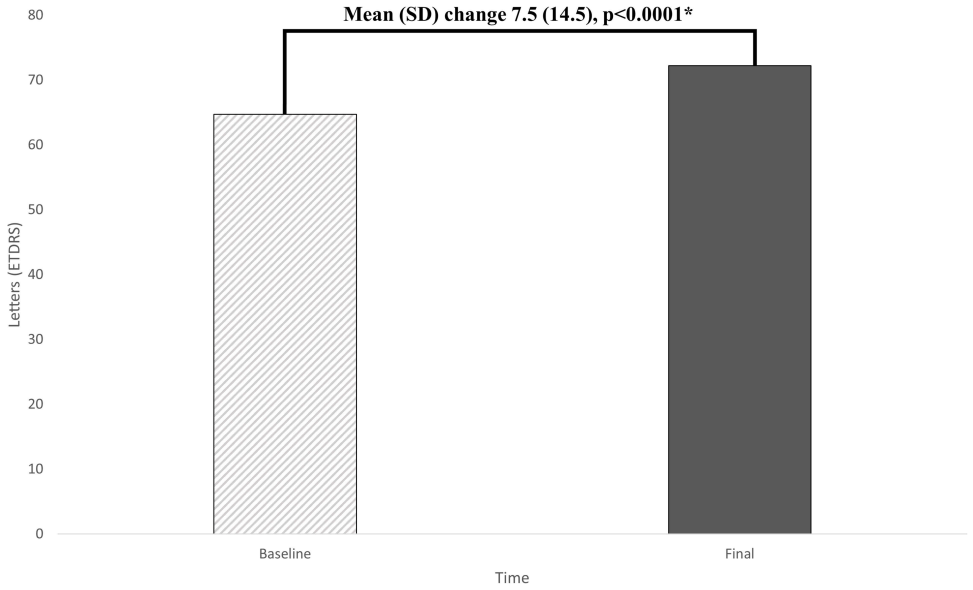

Figure 1 Mean best corrected visual acuity (BCVA) [Early Treatment Diabetic Retinopathy Study (ETDRS) charts] at baseline and at the end of the study. *Statistical significance was determined using the two-way paired Student's *t*-test.

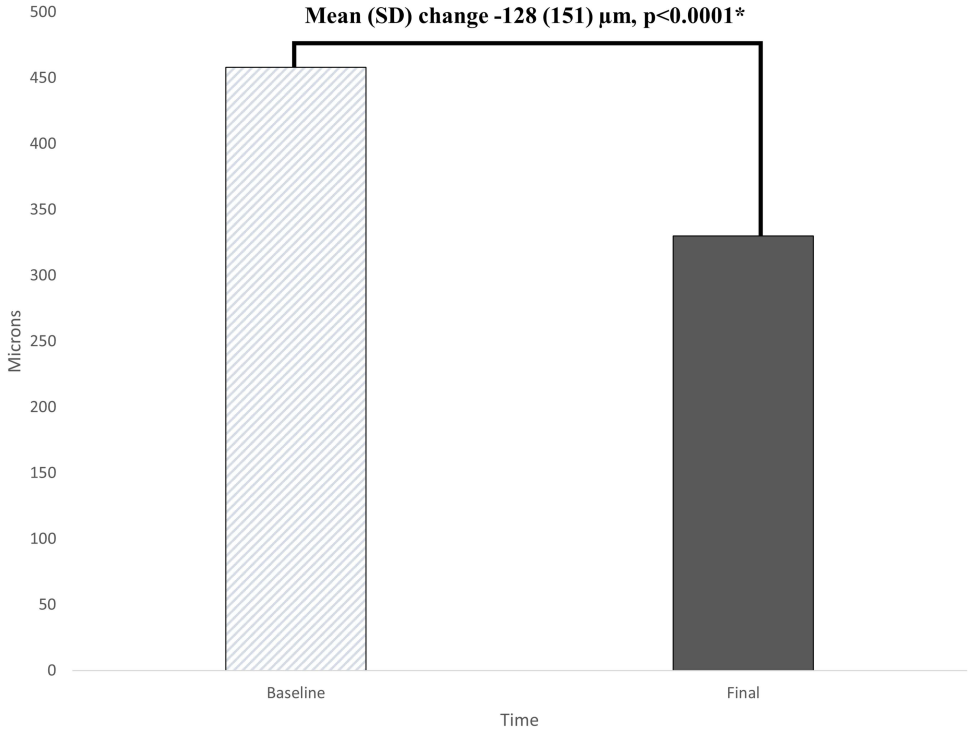

Figure 2 Mean central macular thickness (CMT) at baseline and at the end of the study. *Statistical significance was determined using the two-way paired Student's *t*-test.

the proportion of DEX achieving an improvement ≥15 letters in BCVA between naïve and previously treated eyes (33.3% vs 22.2%, respectively), although such a difference was not statistically significant (p = 0.1136).

In 3 (1.6%) DEX an IOP ≥ 25 mm Hg was observed and, as compared to baseline, 4 (2.1%) DEX experienced an IOP increased ≥10 mm Hg; all the cases were successfully managed with topical antiglaucoma medication (Table 5). Seven

Table 2 Main Clinical Outcomes

Number	
Eyes Implants	97 192
DEX with BCVA improvement ≥ 15 letters*, n (%)	57 (29.7)
Time for achieving such improvement, days Mean (SD)	82.9 (37.9)
DEX with BCVA improvement ≥ 10 letters, n (%)	84 (43.8)
Time for achieving such improvement, days Mean (SD)	93.6 (38.2)
DEX with BCVA reduction ≥ 15 letters, n (%)	24 (12.5)
Time for achieving such reduction, days Mean (SD)	101.0 (41.6)
DEX with BCVA reduction ≥ 10 letters, n (%)	31 (16.1)
Time for achieving such reduction, days Mean (SD)	101.0 (42.7)
Change in BCVA, letters Mean (SD)	7.5 (14.5)
Time for achieving peak improvement, days Mean (SD)	97.9 (41.1)
Change in CMT, μm Mean (SD)	−128.0 (151.0)
Time for achieving peak improvement, days Mean (SD)	99.6 (41.4)
Number of DEX Mean (SD) Duration of the study, years Mean (SD)	1.8 (0.9) 2.1 (1.0)

Notes: *Letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) charts.
Abbreviations: DEX, intravitreal dexamethasone implant; BCVA, best corrected visual acuity; SD, standard deviation; CMT, central macular thickness.

eyes had new onset lens opacity or progression of an existing opacity during the study follow-up (Table 5).

Discussion

According to the results of the current study, receiving an additional DEX and a DME duration <6 months was significantly and positively associated with the probability of achieving a BCVA improvement ≥15 letters from baseline. Additionally, treatment naïve eyes; eyes with a DME duration <6 months, and those who received an additional DEX showed a significantly greater probability of achieving a BCVA improvement ≥10 letters from baseline.

Due to its good efficacy and safety profile,[8–16] DEX has become a first-line therapy for treating patients with DME.

About such a point, the results of our study, did not significantly differ from those previously published.[8–16] DEX Ozurdex® was able to significantly improve both functional (BCVA) and anatomical (CMT) outcomes.

Nevertheless, as far as we know, this is the first study evaluating DEX results according baseline characteristics, which might help to predict its efficacy in DME patients.

Comparing our results to that published by Castro-Navarro et al[15] (a retrospective study conducted on Spanish population), we could observe that the mean change in BCVA and CMT found in our study did not significantly differ from that reported by Castro-Navarro et al (5.6 letters ETDRS and 103.2 μm, respectively).

Moreover, our results in BCVA improvement and CMT reduction are in line with a systematic review search evaluating the pharmacological management of DME in real-life observational studies.[22]

Regarding the main outcome (the proportion of DEX achieving an improvement ≥15 letters in BCVA), it is extremely difficult to compare our results with the currently available scientific literature.[8–16] All the studies evaluated the proportion of eyes achieving a BCVA improvement, while our study evaluated the proportion of DEX achieving such improvement.

The scientific evidence has suggested a better BCVA improvement in naïve eyes than in previously treated ones,[8–16] in agreement with this finding our study found difference in the mean change in BCVA of 3 letters between naïve and previously treated eyes [8.5±15.2 vs 5.3±12.5 letters ETDRS, respectively], although such a difference was not statistically significant ($p = 0.2729$). Nevertheless, the time for achieving a BCVA improvement ≥15 letters, ≥10 letters or the peak BCVA improvement was significantly shorter in the naïve eyes than in the previously treated ones ($p < 0.0001$, $p = 0.0006$ and $p = 0.0258$, respectively).

This study did not find any relationship between the lens status, DME perfusion status, DME status, or HbA1c levels and the probability of DEX for achieving a BCVA improvement ≥15 letters.

Interestingly, as compared with the first DEX, received an additional DEX was significantly associated with achieving a BCVA improvement ≥15 letters from baseline. From our point of view, this finding is extremely important because it suggested that implanting a second DEX, even

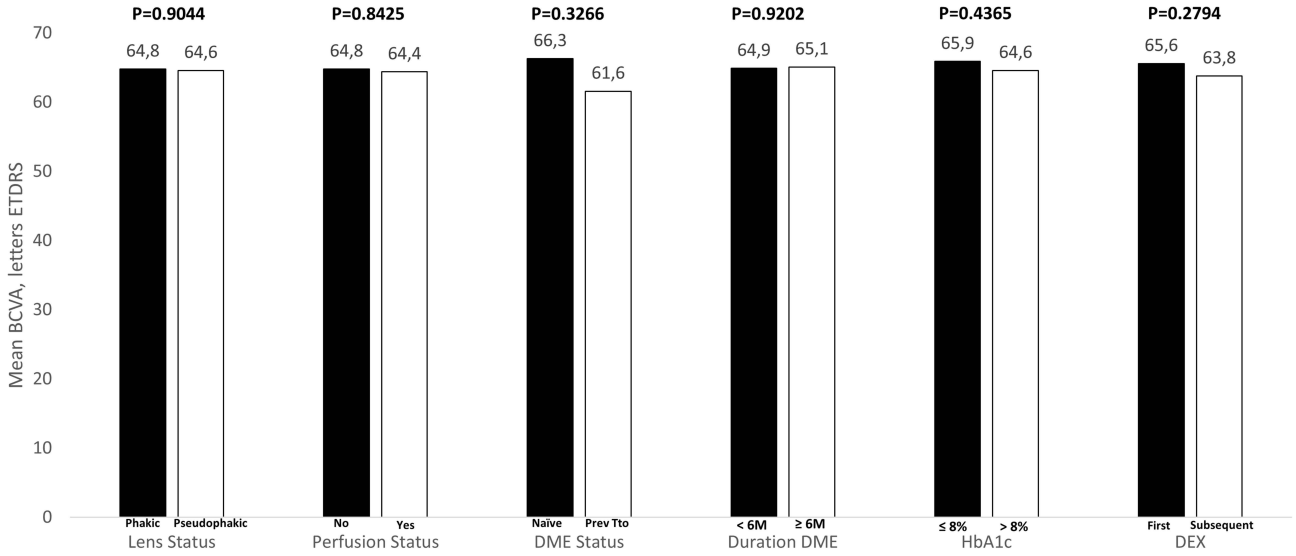

Figure 3 A comparison of baseline best corrected visual acuity among the different groups. P values were calculated by using the two-way independent sample Student *t*-test.
Abbreviations: DME, diabetic macular edema; Prev Tto, previously treated; DEX, intravitreal dexamethasone implant.

in eyes that did not exhibit a good initial respond, might suppose a high probability for obtaining a good functional outcome.

It has been reported that the subsequent DEXs did not have a lower effect, in terms of BCVA improvement, than the first one.[8–16,23] Nevertheless, the results of our study suggested that subsequent DEXs might have even better results than the first DEX.

Additionally, a duration of DME < 6 months has been positively associated with the probability of achieving a

Table 3 Impact of Different Study Variables on Achieving an Improvement in BCVA ≥ 15 Letters

Variables	n	Achieved, %	OR (95 CI)	P value
Lens status				
Phakic*	94	24.5	1.64 (0.88 to 3.07)	0.1225
Pseudophakic	98	34.7		
DME perfusion status				
No*	150	30.7	0.85 (0.41 to 1.79)	0.6766
Yes	42	26.2		
DME status				
Naïve*	129	33.3	0.67 (0.34 to 1.31)	0.2385
Previously treated	63	22.2		
Duration of DME				
<6 months	103	35.9	1.93 (1.02 to 3.67)	0.0434
≥6 months*	85	23.5		
HbA1c				
≤8%*	83	32.5	0.93 (0.51 to 1.69)	0.8156
>8%	99	30.3		
DEX				
First*	97	18.6	2.55 (1.38 to 4.72)	0.0028
Subsequents	95	36.9		

Note: *Reference group. P-values were considered statistically significant at <0.05.
Abbreviations: n, Number; OR, Odds ratio; CI, confidence interval; DME, diabetic macular edema; DEX, intravitreal dexamethasone implant.

Table 4 Impact of Different Study Variables on Achieving an Improvement in BCVA ≥ 10 Letters

Variables	n	Achieved, %	OR (95 CI)	P value
Lens status				
Phakic*	94	39.4	1.42 (0.80 to 2.52)	0.2306
Pseudophakic	98	48.0		
DME perfusion status				
Non-ischemia	150	45.3	1.35 (0.67 to 1.50)	0.4042
Ischemia*	42	38.1		
DME status				
Naïve	129	48.8	2.0 (1.07 to 3.73)	0.0295
Previously treated*	63	33.3		
Duration of DME				
<6 months	103	53.4	2.37 (1.32 to 4.27)	0.0040
≥6 months*	85	34.1		
HbA1c				
≤8%*	83	45.8	0.95 (0.53 to 1.70)	0.8565
>8%	99	44.4		
DEX				
First*	97	34.0	3.04 (1.69 to 5.48)	0.0002
Subsequents	95	47.5		

Notes: *Reference group. P-values were considered statistically significant at <0.05.
Abbreviations: n, Number; OR, Odds ratio; CI, confidence interval; DME, diabetic macular edema; DEX, intravitreal dexamethasone implant.

Table 5 Overview of the Incidence of Adverse Events Over the Course of the Study Follow-Up

Adverse Events (AEs)	All Injections Eyes=97 Injections=192
IOP ≥ 25mm Hg, n (%)	3 (1.6)
Increase of 10 mmHg from baseline, n (%)	4 (2.1)
Use of IOP lowering medication, n (%)	2 (7.1)
Cataract, n (%)	7 (100)
Other related AEs, n (%)	5 (62.5)

BCVA ≥ 15 and ≥10 letters. Our results agreed with those reported by Rosenblatt et al,[16] who found worse functional outcomes in eyes with longstanding DME, which indicated the role of DME duration as a predictor for visual outcomes.

In view of the results, it can be hypothesized that early DME may benefit from early treatment with DEX, although a chronic prolonged DME also respond to DEX.

Our study found that naïve eyes had a better probability for achieving a BCVA improvement ≥10 letters from baseline, this finding did not significantly differ from the currently available evidence.[8–16]

The finding that the proportion of DEX with BCVA reduction ≥10 letters and ≥15 letters were significantly greater in the phakic than in the pseudophakic eyes, from our point of view, would suggest that the reduction of BCVA observed in the phakic eyes might be related with either a new onset lens opacity or progression of an existing opacity during the study follow-up rather than with the efficacy of the DEX itself.

Regarding the adverse events, an IOP ≥ 25 mm Hg was observed in 3 (1.6%) DEX during the course of follow-up. In all cases, increased IOP was managed and controlled with topical medication or observation; none required surgery. These results are similar to those reported in other studies.[9–13,24,25]

There were no new or unexpected adverse events throughout the study.

This study has some limitations that should be taking into account when evaluating its results. The first one is its retrospective design. Although retrospective studies have inherent potential bias, the strict inclusion/exclusion criteria applied in our study might be able to minimize its impact. As a second limitation, it should be mentioned that this is a single center study with the possibility of including a limited number of patients. Nevertheless, the study sample (192 DEX implants administered to 97 eyes of 65 patients) was enough. Another limitation is the lack of

information about the role of OCT data as predictors of DEX outcomes. As aforementioned in the introduction section, different OCT biomarkers have been identified as predictive factors of DEX outcomes.[17–20] Additionally, integrity of external limiting membrane and ellipsoid zone was associated with the final BCVA improvement in patients with DME.[26] Nevertheless, while recognizing the importance of OCT for the clinical management of patients with DME, our study focus on identifying predictive factors beyond OCT.

Conclusions

The results of the current study suggested that eyes who received an additional DEX and those who have a DME duration <6 months have a greater probability of achieving a BCVA improvement ≥15 letters from baseline. Additionally, the probability of achieving a BCVA improvement ≥10 letters from baseline was significantly greater in treatment naïve eyes, eyes with a DME duration <6 months, and those who received an additional DEX. The fact that a DME duration <6 months has been associated with a BCVA improvement ≥15 and ≥10 letters speaks in favor of early treatment of these patients.

This study did not find any relationship between the lens status, DME perfusion status, DME status, or HbA1c levels and the probability of DEX for achieving a BCVA improvement ≥15 letters.

It should be noteworthy that the time for achieving an improvement ≥15 letters, ≥10 letters or the peak improvement was significantly shorter in the naïve eyes than in the previously treated ones.

Finally, the results of this study confirmed previous evidence suggesting that DEX is effective for improving BCVA and CMT in patients with DME.

Further studies, especially prospective, randomized and multicenter studies, are needed to elucidate potential factors associated with success of intravitreal dexamethasone implants in patients with diabetic macular edema.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, agreed to the submitted journal, and agree to be accountable for all aspects of the work.

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Disclosure

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