International Journal of Research Studies in Medical and Health Sciences
Volume 2, Issue 3, 2017, PP 1- 10
ISSN : 2456-6373
http://dx.doi.org/10.22259/ijrsmhs.0203001

Intravitreal Dexamethasone Implant (Ozurdex) for Macular Edema Secondary to Retinal Vein Occlusion

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ABSTRACT

Purpose: *To evaluate the midterm efficacy of the dexamethasone implant injection in eyes with macular edema (ME) associated with retinal vein occlusion (RVO).*

Methods: *Eyes with ME secondary to branch RVO (BRVO) or central RVO (CRVO) treated with an intravitreal dexamethasone implant were analyzed.*

Results: *In thirty-four eyes with BRVO, the median best-corrected-visual-acuity (BCVA) was improved from 0.70 at the baseline to 0.50 logMAR at the final visit (p<0.001). In the CRVO group (ten eyes), the final BCVA was not significantly improved.*

In the BRVO group, the median CMT decreased from 449 at the baseline to 306 microns at the last visit (p<0.001). In the CRVO group, the median CMT increased from 503 at the baseline to 568 microns at the final visit. Twenty eyes with BRVO and seven eyes with CRVO received an additional injection. Laser therapy was applied in seven eyes with BRVO and three eyes with CRVO prior to the reinjection.

Conclusion: *One or two intravitreal dexamethasone implant injections with or without laser therapy may be preferred in eyes with ME secondary to BRVO.*

Keywords: *branch retinal vein occlusion; central retinal vein occlusion; dexamethasone implant; macular edema; Ozurdex implant*

INTRODUCTION

After diabetic retinopathy (DR), retinal vein occlusion (RVO) is the second most common cause of vision loss due to vascular diseases of the retina [1-3]. Branch retinal vein occlusion (BRVO) involving a single vein is the most common type (prevalence of 0.6%–1.1%), whereas central retinal vein occlusion (CRVO) is less common (prevalence of 0.1%–0.4%) [2, 4]. Macular edema (ME) is a common cause of vision loss in both BRVO and CRVO [5]. The pathogenesis of ME in RVO is not completely understood, but it may result from a variety of factors, including hydrostatic effects from increased venous pressure, the presence of inflammatory cytokines (e.g., prostaglandins and interleukin-6), the dysregulation of endothelial tight junction proteins [6], or increased amounts of vascular permeability factors, such as vascular endothelial growth factor (VEGF) [7].

Several therapies have been investigated for the treatment of ME associated with RVO. These include laser photocoagulation (8), the anti-VEGF therapy (ranibizumab) [7, 9, 10], bevacizumab [11, 12], and aflibercept [12, 13] and the corticosteroids triamcinolone acetonide [8, 14, 15] and dexamethasone [16]. Corticosteroids can help to reduce many of the processes thought to play a role in the development of ME in RVO [6, 17-20]. They

have potent anti-inflammatory effects, can reduce vascular permeability, inhibit fibrin deposition and leukocyte movement, suppress homing and migration of inflammatory cells, stabilize endothelial cell tight junctions, and inhibit synthesis of VEGF, prostaglandins, and other cytokines [18]. Intravitreal injections of the lipophilic corticosteroid triamcinolone acetonide have been shown to produce benefits in eyes with RVO, but several adverse events have been noted (with elevated intraocular pressure [IOP] and cataract being the most common) [8, 10, 15, 21-29]. Other corticosteroids, however, have their own unique properties and may have different clinical profiles in intravitreal use [30].

Dexamethasone is a potent, water-soluble corticosteroid that can be delivered to the vitreous cavity using the dexamethasone intravitreal implant (DEX implant; Ozurdex, Allergan, Inc., Irvine, CA). The DEX implant is composed of a biodegradable copolymer of lactic acid and glycolic acid containing micronized dexamethasone. The drug copolymer complex gradually releases the total dose of dexamethasone over a series of months after it is inserted into the eye through a small pars plana puncture using a customized applicator system. In a recent study in eyes with persistent ME resulting from several different causes (including RVO), a 0.7-mg DEX implant produced improvements in visual acuity, macular thickness, and fluorescein leakage that were sustained for up to 6 months [16].

The purpose of the current study was to evaluate the midterm efficacy and safety of the DEX implant in eyes with vision loss due to ME associated with RVO.

METHODS

In this prospective, interventional study all participants provided their written informed consent. The study adhered to the principles of the Declaration of Helsinki. Patients with ME secondary to BRVO or non-ischemic CRVO who were treated with an intravitreal DEX implant were evaluated.

The inclusion criteria were as follows: the presence of ME following CRVO or BRVO with an onset within the previous 3 months; no previous therapy; a best-corrected visual acuity (BCVA) ≥20/400 Snellen; a central macular thickness (CMT) ≥250 μm confirmed by spectral domain-optical coherence tomography (SD-OCT -Cirrus HD-OCT model 5000; Carl Zeiss Meditec, Dublin, California, USA) and a follow-up of at least 12 months.

The main exclusion criteria included the following: clinically significant epiretinal membrane, vitrectomy prior to the injection, the presence of DR or diabetic ME, retinal or optic disc neovascularization, active or history of choroidal neovascularization, presence of rubeosis iridis, active infection, aphakia or anterior-chamber intraocular lens, clinically significant media opacity, glaucoma or current ocular hypertension requiring medication to control IOP in the study eye, or history of a steroid-induced IOP increase in either eye. Patients were also excluded if they had an uncontrolled systemic disease or were currently using or anticipated using systemic steroids or anticoagulants during the study.

Follow-up visits were performed at 1, 3, 6, 9 and 12 months after injection of the DEX implant. IOP was measured with Goldmann applanation tonometry, and CMT was measured with SD-OCT. The main outcome measures were BCVA, CMT and IOP. CMT was defined as the distance between the inner retinal boundary (internal limiting membrane) and outer retinal boundary (outer border of the photoreceptors) in the foveal area.

Intravitreal Dexamethasone Implant Injection

All intravitreal injections were performed in the operating room under sterile conditions. The eye was anaesthetized with topical anesthetics, and preoperative antisepsis was performed according to standard clinical practice. Next, 0.7 mg of dexamethasone was injected intravitreally through the pars plana using a 22-gauge applicator. Retreatment was based on an open pro re nata (PRN) regime (significant decline in the BCVA, as demonstrated by a loss of at least one line, or an increased CMT of 150 microns was noticed) [31]. Additionally, some patients received complementary sectoral or panretinal photocoagulation to ischemic areas according to the individual retinal perfusion status and the retinal angiography at the 6-month follow-up visit.

Retreatment

A significantly decreased BCVA and recurrent ME were noticed in twenty-one of thirty-four eyes with BRVO during the follow-up period.

Early retreatment prior to the labeled 6-month interval was supported by the covering insurance company of the affected patient in twenty-one eyes of thirty-four initially treated eyes (61.7%). A loss of 5 letters (4 eyes) and recurrent CME (17 eyes) were noticed in 21 of 34 eyes. Of these, one eye (4.76%) received an anti-VEGF injection and 20 (95.24%) received a second intravitreal DEX implant according to the physician's discretion. Seven eyes (20.58%) received a sectoral laser photocoagulation prior to the second implant injection.

In the CRVO group, a significantly decreased BCVA and recurrent ME were noticed in seven of ten eyes during the follow-up period. Early retreatment was covered by the insurance company or preferred by affected patients in seven of ten initially treated eyes (70%). A loss of 5 letters (0 eyes) and recurrent CME (7 eyes) were noticed in 7 of 10 eyes with CRVO during the follow-up period. These seven eyes (100%) were treated with a second intravitreal Ozurdex injection based on the physician's discretion. Three eyes (30%) received a panretinal laser photocoagulation due to retinal ischemia prior to the second implant injection.

Statistics

Changes between CMT values (as a continuous variable) obtained in clinical visual testing at each time-point were analyzed using paired t-tests, and the changes between visual acuity values (as a discrete variable) at the same time-points were analyzed using Friedman's two-way analysis of variance by ranks. The extent to which the disease duration prior to the initial Ozurdex injection affected the study outcomes was analyzed using a repeated-measures analysis of variance (ANOVA). Differences in the patients' characteristics at baseline (regarding age, BCVA and CMT) were assessed using an unpaired t-test. Statistical analyses were performed using IBM SPSS Statistics version 21.0. P-values <0.05 were required for statistical significance.

RESULTS

Forty-four patients with ME secondary to BRVO (n= 34) or CRVO (n=10) who were treated with intravitreal DEX implant were included in the study. The patient characteristics are shown in **Table 1**.

Table1. *Patients characteristics at baseline prior to the first intravitreal injeciton of 0.7 mg dexamethasone implant. CRVO, Central Retinal Vein Occlusion; BRVO, Branch Retinal Vein Occlusion; SD, Standard Deviation; BCVA, best corrected visual acuity.*

Variable	CRVO	BRVO
Number of patients	10	34
Number of males	7	14
Mean age (SD)(years)	70.1±7.07	62.4±7.73
Median logMAR BCVA (SD)	0.70 (0.70-1.35)	0.70 (0.50-1.0)
Mean central retinal thickness (SD), micron	540±168 (360-824)	467±113 (260-645)

The effects of the intravitreal dexamethasone therapy were analyzed separately for BRVO and CRVO.

In eyes with BRVO, treatment with an intravitreal DEX implant resulted in a significant improvement in the median BCVA (p<0.001), which decreased from 0.70 logMAR at baseline to 0.50 logMAR at 12 months after the implant. The median BCVA maintained was significantly better (p<0.001) than the baseline BCVA at each follow-up visit.

Table2. *The comparison of the best-corrected visual acuities (BCVA) in logMAR (logarithm of the minimum angle of resolution) in branch retinal vein occlusions at different visits using* Friedman's Two-way *Analysis of Variance by* Ranks*. The minimum and maximum values are given in parenthesis along with the means. The 25th and 75th percentile values are given in parentheses along with the medians. *p<0.05; MC= multiple comparisons.*

Visit time	Mean BCVA	Median BCVA	p value	Significant MC*
Preinjection (0)	0.80±0.41 (0.22-1.80)	0.70 (0.50-1.0)	<0.001*	0 vs 1 (p<0.001) 0 vs 3 (p=0.004) 0 vs 6 (p=0.006) 0 vs 9 (p<0.001) 0 vs 12 (p=0.011)
At 1st m (1)	0.49±0.29 (0.10-1.30)	0.45 (0.28-0.70)		
At 3rd m (3)	0.53±0.31 (0.10-1.50)	0.45 (0.36-0.70)		
At 6th m (6)	0.55±0.37 (0.10-1.50)	0.50 (0.30-0.70)		
At 9th m (9)	0.54±0.35 (0.10-1.30)	0.50 (0.22-0.78)		
At 12th m (12)	0.60±0.38 (0.10-1.50)	0.50 (0.30-1.00)		

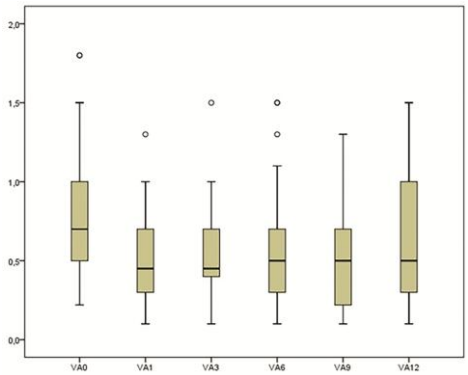

Figure1. *The change in BCVA with the view box plot graphs at BRVO.*

In eyes with CRVO, injection of an intravitreal DEX implant induced significant visual improvements of the median BCVA (p<0.009), from 0.70 logMAR at baseline to 0.50 and 0.70 logMAR at 3 and 6 months, respectively. The final median BCVA maintained was not significantly improved compared to the initial BCVA. **Table 3 and Figure 2**

Table3. *The comparison of the best-corrected visual acuities (BCVA) in logMAR (logarithm of the minimum angle of resolution) in central retinal vein occlusions at different visits using Friedman's Two-way Analysis of Variance by Ranks. The minimum and maximum values are given in parenthesis along with the means. The 25th and 75th percentile values are given in parentheses along with the medians. *p<0.05; MC= multiple comparisons*

Visit time	Mean BCVA	Median BCVA	p value	Significant MC*
Preinjection (0)	0.93±0.37 (0.50-1.50)	0.70 (0.70-1.35)	0.009*	0 vs 3 (p=0.042) 0 vs 6 (p=0.035)
At 1st m (1)	0.74±0.40 (0.22-1.50)	0.65 (0.40-1.03)		
At 3rd m (3)	0.67±0.38 (0.10-1.50)	0.50 (0.50-0.93)		
At 6th m (6)	0.70±0.41 (0.05-1.50)	0.70 (0.45-1.00)		
At 9th m (9)	1.00±0.80 (0.30-0.48)	0.85 (0.48-1.20)		
At 12th m (12)	0.84±0.39 (0.40-1.50)	0.85 (0.48-1.15)		

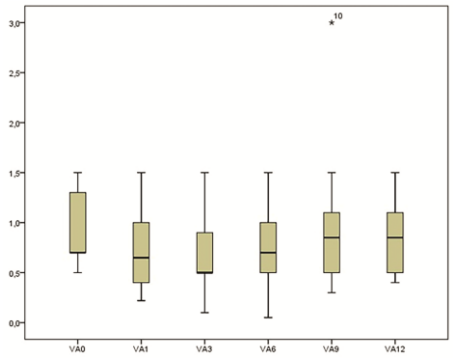

Figure2. *The change in BCVA with the view box plot graphs at CRVO.*

In eyes with ME secondary to BRVO, the median CMT decreased from 449 micron (µm) at baseline to 306 µm at 12 months. The median CMT was significantly less than the baseline CMT at each follow-up visit (p<0.001).

Table4. *The comparison of the central macular thickness (CMT) in branch retinal vein occlusions at different visits using* Friedman's Two-way *Analysis of Variance by* Ranks. *The minimum and maximum values are given in parenthesis along with the means. The 25th and 75th percentile values are given in parentheses along with the medians. *p<0.05; MC= multiple comparisons.*

Visit time	Mean CMT (µm)	Median CMT (µm)	p value	Significant MC*
Preinjection (0)	467±113 (260-645)	449 (373-569)	<0.001*	0 vs 1 (p<0.001) 0 vs 3 (p<0.001) 0 vs 9 (p<0.001) 0 vs 12 (p<0.001) 1 vs 6 (p<0.001) 1 vs 12 (p=0.003) 3 vs 6 (p=0.010) 6 vs 9 (p=0.005)
At 1st m (1)	258±76 (143-480)	250 (193-310)		
At 3rd m (3)	277±74 (168-449)	267 (222-314)		
At 6th m (6)	392±124 (188-694)	373 (297-475)		
At 9th m (9)	308±121 (189-617)	253 (226-351)		
At 12th m (12)	358±142 (204-652)	306 (234-485)		

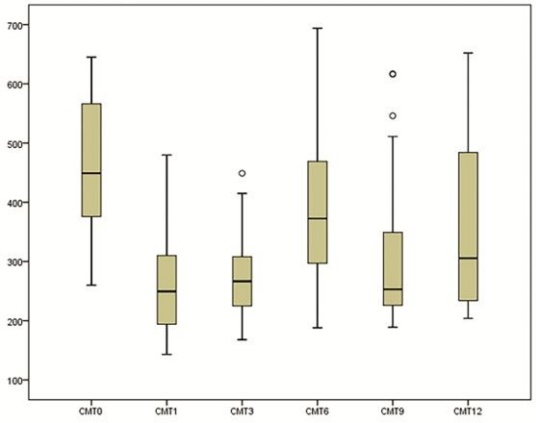

Figure3. *The change in CMT with the view box plot graphs at BRVO.*

In CRVO, the median CMT maintained was significantly reduced compared with the baseline at the first two follow-up visits (p<0.001). However, the median CMT increased from 503 µm at the baseline to 568 µm at 12 months.

Table5. *The comparison of the central macular thickness (CMT) in central retinal vein occlusions at different visits using* Friedman's Two-way *Analysis of Variance by* Ranks. *The minimum and maximum values are given in parenthesis along with the means. The 25th and 75th percentile values are given in parentheses along with the medians. *p<0.05; MC= multiple comparisons.*

Visit time	Mean CMT (µm)	Median CMT (µm)	p value	Significant MC*
Preinjection (0)	540±168 (360-824)	503 (378-714)	<0.001*	0 vs 1 (p<0.001) 0 vs 3 (p=0.008) 1 vs 12 (p=0.005)
At 1st m (1)	224±73 (192-222)	201 (192-222)		
At 3rd m (3)	311±230 (156-902)	212 (195-350)		
At 6th m (6)	421±175 (204-725)	394 (265-571)		
At 9th m (9)	355±150 (186-659)	313 (240-463)		
At 12th m (12)	496±218 (226-780)	568 (242-691)		

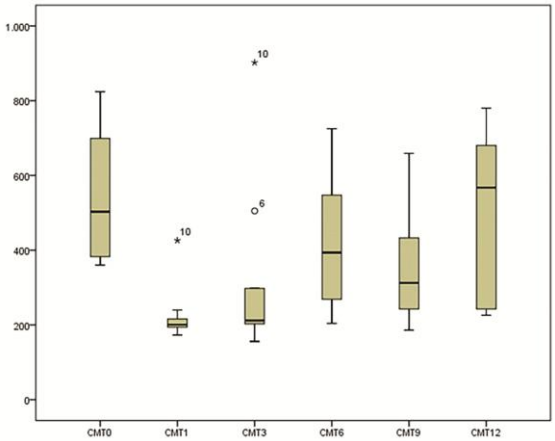

Figure4. *The change in CMT with the view box plot graphs at CRVO.*

No major ophthalmologic (retinal detachment, uveitis, endophthalmitis, retinal artery occlusion) or systemic (thromboembolic events, systemic hypertension, myocardial infarction) side effects occurred.

A high IOP over 21 mmHg was noted in ten patients in the BRVO group (29.4%) and in two patients in the CRVO group (20%) during the 12 months of follow-up time. IOP elevation was controlled by medical therapy in all patients.

A statistically significant increase in IOP was observed at months 1, 3 and 9 in the BRVO group compared to the baseline values. However, there was no significant difference in IOP at the 6th and 12th month compared to the initial values. There was no statistically significant change in the mean IOP in the CRVO group at any visit. The mean and median IOP changes are shown in the tables for the BRVO and CRVO groups.

Table6. *The comparison of the intraocular pressure (IOP) in branch retinal vein occlusions at different visits using* Friedman's Two-way *Analysis of Variance by* Ranks*. The minimum and maximum values are given in parenthesis along with the means. The 25th and 75th percentile values are given in parentheses along with the medians. *p<0.05; MC= multiple comparisons.*

Visit time	Mean IOP (mmHg)	Median IOP (mmHg)	P value	Significant MC*
Preinjection (0)	15±3 (9-21)	14 (13-16)	<0.001*	0 vs 1 (p=0.005) 0 vs 3 (p=0.035) 1 vs 6 (p=0.004) 1 vs 12 (p=0.025) 3 vs 6 (p=0.031)
At 1st m (1)	17±4 (11-32)	17 (14-19)		
At 3rd m (3)	17±5 (9-36)	16 (14-19)		
At 6th m (6)	15±2.6 (9-20)	15 (13-16)		
At 9th m (9)	17±5 (11-38)	16 (14-18)		
At 12th m (12)	15±2 (10-22)	15 (13-16)		

Table7. *The comparison of the intraocular pressure (IOP) in central retinal vein occlusions at different visits using* Friedman's Two-way *Analysis of Variance by* Ranks*. The minimum and maximum values are given in parenthesis along with the means. The 25th and 75th percentile values are given in parentheses along with the medians.*

Visit time	Mean IOP (mmHg)	Median IOP (mmHg)	p value
Preinjection (0)	14±3 (8-19)	14 (11-16)	>0.05
At 1st m (1)	17±4 (12-23)	16 (13-22)	
At 3rd m (3)	15±3 (10-20)	16 (12-18)	
At 6th m (6)	14±3 (8-18)	14 (13-15)	
At 9th m (9)	16±3 (11-20)	15 (14-18)	
At 12th m (12)	17±8 (10-38)	14 (13-18)	

During follow-up, cataracts were reported as adverse events in four of twenty-eight phakic eyes (14.2%) in the BRVO group and one of seven phakic eyes (14.2%) in the CRVO group. Five patients had a surgical procedure for cataract in the study eye (four eyes in the BRVO group and one eye in the CRVO group).

DISCUSSION

Ozurdex is the first drug approved for the treatment of ME in RVO that may offer patients a long-lasting relief from their visual symptoms and macular edema with a limited number of required follow-up visits [32, 33]. In this study, we evaluated the effects of intravitreal Ozurdex treatments administered on a PRN regime for RVO. Overall, we found sustained functional (BCVA) and morphological (CMT) improvements in eyes with BRVO. We also obtained an improvement in CRVO cases in the initial visits, but the final outcomes were not different from the preinjection values. These findings support previous observations that CRVO is a more visually disabling disorder than BRVO [34, 35].

In the current study including thirty-four BRVO cases, the visual improvement was significant from the initial visits to the last visit. In 61.7% of our cases, an additional injection was required. The multicenter GENEVA trial was the first study to assess the clinical effects of Ozurdex injections after its approval in a clinical routine setting [36]. The trial examined eyes with ME after an intravitreal Ozurdex injection on a monthly basis. Treatment with intravitreal dexamethasone injections led to a significant improvement in the BCVA and a decrease in the CMT in all RVO eyes, which were observed as early as 1 month after the injection. The peak functional and anatomical efficacy was observed at 2 months. From 3 months on, a moderate decline in the BCVA was noticed. The cumulative response rate was 41% in the 0.7 mg group, 40% in the 0.35 mg group, and 23% in the sham group (p=0.001). Although the proportion of eyes achieving at least a 15-letter improvement from the baseline BCVA was greater in the treatment groups at month 1 (21% in the 0.7 mg group vs 18% in the 0.35 mg group vs 8% in the sham group; p=0.001) and month 3 (22% in the 0.7 mg group vs 23% in the 0.35 mg group vs 13% in the sham group; p=0.001), this effect was no longer statistically significant at month 6 [35]. Among the patients who received two treatments with the 0.7-mg DEX implant in the GENEVA study (12 months), BCVA improvements were similar after the first and second injections. Overall, as well as in the subgroups of study eyes diagnosed with BRVO and CRVO, the peak improvement in the mean BCVA was approximately 10 letters and occurred 60 days after each injection. At least a 15-letter improvement in BCVA from the

baseline was observed in up to 30% of eyes in the DEX 0.7/0.7 group at visits during the masked phase of the study (the first 6 months) and in up to 32% of eyes in the DEX 0.7/0.7 group at visits during the open-label phase of the study (the second 6 months) [36].

In a retrospective report by Bezatis et al. that included eyes with BRVO, treatment with an intravitreal DEX implant resulted in a significant improvement in the median BCVA ($p<0.001$), increasing from 0.6 logMAR at baseline to 0.45 logMAR after 6 months. The median BCVA maintained was significantly better ($p<0.001$) compared with the baseline at each follow-up visit [27]. These findings are consistent with those from our present study. Alshahrani et al. conducted a study involving fourteen BRVO cases, and there was a statistically significant improvement in BCVA at the 3rd month. However, the improvement was not maintained at the 6-month visit [37].

In the current study, the decrease in CMT was significant in all visits compared to the initial CMT. This was consistent with the improvement in BCVA. The mean CMT maintained during the first and second visits (at months 1 and 3) was a reduced thickness of 209 and 190 microns, respectively, and there was a moderate increase during the following visits. Consistent with our findings, the GENEVA study reported that the mean CMT obtained during the first and second visits was a reduced thickness of 220 and 239 microns, respectively, while there was a moderate increase during the following weeks [35]. Bezatis et al. reported that the mean CMT maintained was significantly reduced ($p<0.001$) compared with the baseline at each follow-up visit [31]. In a study by Alshahrani et al., the mean baseline CMT was 490.86 ± 133.94 µm in eyes with BRVO. The mean CMT decreased significantly to 259.00 ± 37.56 µm at the 1-month visit and to 340.29 ± 112.93 µm at the 3-month visit ($p=0.001$ and $p=0.01$, respectively). However, the difference was not statistically significant at the 6-month visit ($p=0.177$) [37].

In the current study including ten CRVO cases, the outcomes were not satisfactory. We tried a second injection in seven cases (70%), but the final BCVA was still not significantly different from the preinjection values. In the GENEVA study, the mean change in VA from the baseline in patients with CRVO was approximately +2.2 letters for retreated patients and −1.2 letters for delayed treatment patients (32). Bezatis et al. found a significant visual improvement of the mean BCVA from 0.7 logMAR at the baseline to 0.52 logMAR after 6 months following the injection in eyes with CRVO. The median BCVA remained significantly better ($p<0.001$) when compared with the baseline at each follow-up visit [31]. Alshahrani et al. observed an initial improvement in BCVA for thirteen CRVO patients following the injection at visits in the 1st and 3rd months. However, the improvement was not maintained at the 6-month visit [37]. In our study, the decrease in CMT was initially significant compared to the baseline CMT, but this was not compatible with our functional outcomes. The mean CMT decreased from the baseline 540±168 to 496±218 µm at the 12-month visit. Bezatis et al. reported a significant decrease in CMT at all visits [31]. Alshahrani et al. also showed a significant decrease in CMT in CRVO patients at visits in the 1st, 3rd and 6th month. At 6 months, there was a statistically significant decrease in CMT from the baseline value of 656.31 ± 220.19 µm to 466.41 ± 316.17 µm ($p=0.033$) [37].

It was reported that IOP elevation and cataract are the most common complications after the intravitreal Ozurdex implant injection. In our series, IOP elevation was noted in 29.4% of the eyes with BRVO and 20% of the eyes with CRVO. Fortunately, the mean IOP levels were not different at the last visit in both groups. In the literature, IOP elevation was noted in 4% to 53% of cases with RVO after the intravitreal Ozurdex implant injection [35-39]. We operated on all of our cases in which cataract developed after the injection. Our percentage of cases that developed cataract was consistent with those reported in the literature. Cataract developed in 1.8% to 29.8% of the eyes with RVO after the intravitreal Ozurdex implant injection [31-33]. In the GENAVA (twelve months) study, 25.5% of the cases in the dexamethasone 0.7/0.7 mg group, 25.0% in the dexamethasone 0.35/0.7 mg group, and 28.1% in the sham/dexamethasone 0.7 mg group received medical treatment for IOP compared to 0% in the 0.35 mg/no implant group and the sham/no implant group. The cataract progression varied and was reported at 5.7% in the sham/no implant group, 10.5% in the sham/0.7 mg group and 29.8% in 0.7/0.7 mg dexamethasone-treated patients [36].

Our study has several limitations. It was an uncontrolled study conducted in a single-center

institutional setting and included a relatively small study population of CRVO cases. This precluded any definitive estimation of the efficacy or safety of intravitreal Ozurdex injection. The retreatment criterion of the OCT of 150 microns may be large. We could speculate that, the outcomes would be better, if our retreatment criterion was below 150 microns. Not all patients could be immediately retreated in our routine clinical setting because some insurance companies required the completion of an entire 6-month follow-up period before an additional retreatment could be assigned. The GENEVA study prohibited panretinal laser photocoagulation to solely investigate the effects of the intravitreal Ozurdex injection. We conducted a prospective study with one year of follow-up. In our current trial, additional laser photocoagulation was applied in selected cases, and this could possibly reduce the progression of the disease [40]. However, Spaide et al. reported that laser photocoagulation to peripheral areas of nonperfusion did not result in either decreased injection frequency or improved visual acuity in eyes with CRVO treated with ranibizumab [41].

CONCLUSION

Based on our monthly examinations, a significant visual improvement and reduction in CMT was noticed at all visits in the BRVO cases in one year of follow-up. In the CRVO cases, the anatomical improvement was maintained, but the visual outcome was not satisfactory. Better outcomes could be obtained, if patients were reevaluated earlier than 6 months and treated again if necessary.

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Citation: *Mustafa Deger B, Nazmiye E, Huseyin G, Erdogan Y, Emre T, Ertugrul C. Intravitreal Dexamethasone Implant (Ozurdex) for Macular Edema Secondary to Retinal Vein Occlusion. International Journal of Research Studies in Medical and Health Sciences. 2017;2(3):1-10.*