Annals of Medical Research
DOI: 10.5455/annalsmedres.2018.11.260 2019;26(2):255-9

Original Article

The clinical outcomes of intravitreal dexamethasone implant as the first-line treatment in retinal vein occlusion related macular edema

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Abstract

Aim: To investigate the alterations in central macular thickness (CMT), best-corrected visual acuity (BCVA) and intraocular pressure (IOP) after intravitreal dexamethasone implant (IDI; Ozurdex) injections in patients with treatment-naive central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO)-related macular edema in clinical practice.

Material and Methods: Totally 41 eyes of 41 patients diagnosed with BRVO or CRVO, who were treatment-naive and treated with only intravitreal dexamethasone implants, were retrospectively investigated. Anterior and posterior segment examinations were performed with a slit lamp bio-microscope. BCVA was assessed using Snellen chart and then converted to logarithm of minimum angle of resolution (log MAR) units before statistical analysis and CMT measurements were performed with spectral domain optical coherence tomography.

Results: The mean age of patients was 65.95 ±6.164 years (range: 51-78). Central retinal vein was occluded in 14 patients while branches were occluded in remaining 27 patients. The patients were followed for 14.93±1.942 months (median: 15, range: 12-20 months). The mean number of injections was 2.83±0.803 (median: 3, range: 1-4). BCVA was significantly better in all time periods after treatment (p: 0.001). There was a significant decrease in CMT in all time periods after treatment compared with pre-treatment values (p: 0.001). During follow-up period, IOP was determined to be higher than 25 mm-Hg in 5 patients, and cataract was diagnosed in 6 patients.

Conclusion: Intravitreal dexamethasone injection is an effective mode of treatment in patients with RVO-associated macular edema. Its side effects are not severe or common. However the patients should be kept under follow-up for recurrences.

Keywords: Dexamethasone; Optical Coherens Tomography; Retinal Vein Occlusion.

INTRODUCTION

Retinal vein occlusion (RVO) is a common cause of altered vision especially in elderly patients. Increased intraluminal pressure and vascular endothelial damage associated with RVO results in macular edema. Proinflammatory cytokines are also involved in augmentation of macular edema (1,2).

In treatment of RVO-related macular edema intraocular injections of anti-inflammatory drugs such as corticosteroids or antagonists of vascular endothelial growth factor (VEGF) are in clinical use. Corticosteroids have anti-angiogenic and anti-inflammatory effects and regarding these properties, they are commonly in use for the treatment of both CRVO and BRVO-related macular edemas. Nevertheless, some complications of these injections are also clearly known such as cataract or steroid-related increase in intraocular pressure (IOP). Moreover, they have short-term effects and repeated injections may be required (3-5).

The slow-release intravitreal dexamethasone implant 0.7 mg (DEX implant; Ozurdex®, Allergan plc, Dublin, Ireland) has been shown to be effective in treating macular edema secondary to RVO (6,7).

In this study, we aimed to investigate the alterations in central macular thickness (CMT) intraocular pressure (IOP), and best-corrected visual acuity (BCVA) and clinical outcomes after IDI injections in previously untreated patients with BRVO or CRVO-related macular edema.

MATERIAL and METHODS

Totally 41 patients diagnosed with BRVO or CRVO, who were previously untreated and treated with only intravitreal

Received: 21.11.2018 **Accepted:** 11.12.2018 **Available online:** 13.12.2018
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dexamethasone implants in Erzincan Mengücek Gazi Education and Research Hospital between January 2015 and September 2018 were retrospectively investigated. Follow-up data were obtained from patient files. The study was approved by Erzincan Binali Yıldırım University Clinical Research Ethics Commıttee (33216249-604.01.02-E.49616).

Patients with retinal vascular diseases other than RVO, uveitis, age-related macular degeneration, glaucoma, diabetic retinopathy, a history of eye trauma, or ocular surgery other than cataract operations were excluded from the study.

All patients included in the study underwent a complete ophthalmic examination. Anterior and posterior segment examinations were performed with a slit lamp bio-microscope. Goldmann applanation tonometer was used for the IOP measurement. BCVA was assessed using Snellen chart and then converted to logarithm of minimum angle of resolution (log MAR) units before statistical analysis. Fundus fluorescein angiography (FFA) was performed with Visucam 500 (Carl Zeiss Meditec, Jena, Germany), and CMT measurements was performed with spectral domain optical coherence tomography (RS-3000 Advance, Nidek, Padova, Italy).

In each patient, IDI (Ozurdex, 0.7 mg; Allergan, Inc., Irvine, CA, USA) was performed by the same surgeon in the operating room at superior temporal quadrant, 3.0–4.0 mm distance from the limbus using a single-use 22-gauge applicator. In our clinic, in routine practice, after IDI injections, Eye drops with 0.3% ofloxacin four times a day for seven days is prescribed to all patients and the patients are followed monthly for adverse effects and recurrences. During follow-ups, patients with an IOP measurement >25 mmHg are treated medically; and in that period if cataract develops, patients are operated.

Statistical Analysis

SPSS version 21.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used for statistical analyses of measurements. Descriptive statistics (mean± standard deviation, median, range) were performed to determine the clinical outcomes of study participants. Paired Student's t-test was used to compare the measurements obtained at two different time points. P values less than 0.05 was defined as statistically significant.

RESULTS

Totally 41 patients (23 females, 18 males) diagnosed with RVO (14 CRVO, 23 BRVO) with a mean age of 65.95 ±6.164 years (median: 67, range: 51-78 years) were met the inclusion criteria. Among those patients, right eyes were treated in 17 patients and left eyes were treated in remaining 24 patients. Central retinal vein was occluded in 14 patients while branches were occluded in remaining 27 patients. The patients were followed for 14.93±1.942 months (median: 15, range: 12-20 months). The mean number of injections was 2.83±0.803 (median: 3, range: 1-4). The second injection was performed (n: 38) on the 5.58 ±1.004 month (median: 5, range:4-9), while the third injection was performed (n:31) on the 11.32±0.98 months (median:11 range: 9-13), and the forth injection was performed (n:8) on the 15.50 ± 1.41 (median: 16 range: 13-17).

In Table 1, alterations in intraocular pressure of patients during follow-up period are summarized. In that period, statistically significant increase in IOP was observed only at the end of the first month (p: 0.001) (Figure 1). Alterations in BCVA values in that period are summarized in Table 2. Regarding these findings, visual acuity was better in all time periods after treatment (p: 0.001) (Figure 2). Alterations in CMT of patients during follow-up are summarized in Table 3. There was a significant decrease in CMT in all time periods after IDI injections (p: 0.001) (Figure 3).

During follow-up period, intraocular pressure was determined to be higher than 25 mm-Hg in 5 patients (3 in CRVO and 2 in BRVO groups) and treatment was started. During this period, cataract was diagnosed in 6 patients (3 in CRVO and 3 in BRVO groups) and they were operated. There were not any complications reported associated with the cataract surgery in these patients.

Table 1. Alterations in intraocular pressure of patients during follow-up

	Mean ± Standard deviation	Median (Range)
Preoperative (n:41)	15.32 ±2.173	15 (12 -20)
1st month (n:41)	18.15±5.769	16 (13-35)
2nd month (n:41)	15.85±2.445	15 (13-22)
3rd month (n:41)	15.61±2.036	15 (13-21)
4th month (n:41)	15.02±2.208	15 (12-21)
5th month (n:41)	15.02±1.956	15 (12-20)
6th month (n:41)	15.05±1.910	15 (11-21)
7th month (n:41)	15.05±2.247	14 (11-22)
8th month (n:41)	14.78±2.275	14 (11-20)
9th month (n:41)	14.78±2.231	14 (12-20)
10th month (n:41)	14.73±2.247	15 (11-22)
11th month (n:41)	14.98±2.230	14 (12-21)
12th month (n:41)	15.10±2.385	14 (12-23)
13th month (n:38)	14.97±1.910	15 (12-21)
14th month (n:31)	15.00±1.571	15 (12-20)
15th month (n:20)	14.95±2.212	14.5 (11-21)
16th month (n:14)	14.93±2.336	14.5 (12-19)
17th month (n:8)	15.13±2.696	14.5 (11-19)
18th month (n:5)	15.60±2.302	16 (12-18)
19th month (n:2)	16.00±1.414	16 (15-17)
20th month (n:1)	16.00	16

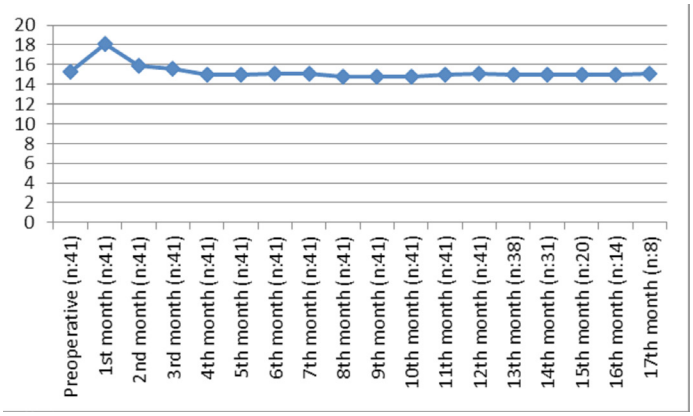

Figure 1. Alterations in intraocular pressure of patients during follow-up

Table 2. Alterations in BCVA of patients during follow-up

	Mean ± Standard deviation	Median
Preoperative (n:41)	0.83±0.288	0.69
1st month (n:41)	0.49±0.266	0.39
2nd month (n:41)	0.37±0.233	0.30
3rd month (n:41)	0.38±0.275	0.22
4th month (n:41)	0.43±0.271	0.30
5th month (n:41)	0.53±0.337	0.52
6th month (n:41)	0.54±0.288	0.52
7th month (n:41)	0.45±0.255	0.39
8th month (n:41)	0.42±0.247	0.30
9th month (n:41)	0.44±0.256	0.36
10th month (n:41)	0.45±0.269	0.30
11th month (n:41)	0.52±0.280	0.39
12th month (n:41)	0.52±0.284	0.52
13th month (n:38)	0.43±0.233	0.39
14th month (n:31)	0.41±0.246	0.30
15th month (n:20)	0.47±0.260	0.39
16th month (n:14)	0.58±0.323	0.52
17th month (n:8)	0.52±0.342	0.35
18th month (n:5)	0.54±0.309	0.39
19th month (n:2)	0.50±0.231	0.50
20th month (n:1)	0.39	0.39

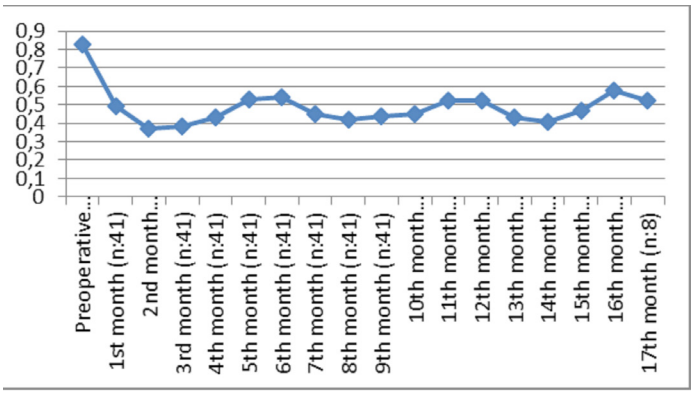

Figure 2. Alterations in BCVA of patients during follow-up

Table 3. Alterations in CMT of patients during follow-up

	Mean ± Standard deviation	Median
Preoperative (n:41)	648.34±155.974	602.00 (398-986)
1st month (n:41)	309.56±48.240	302.00 (212-456)
2nd month (n:41)	273.93±37.480	272.00 (198-348)
3rd month (n:41)	281.05±40.588	285.00 (184-356)
4th month (n:41)	307.95±91.766	292.00 (186-612)
5th month (n:41)	414.05±111.027	316.00 (198-884)
6th month (n:41)	388.34±89.473	326.00 (192-678)
7th month (n:41)	322.27 ±73.357	312.00 (189-524)
8th month (n:41)	315.59±81.257	298.00 (192-688)
9th month (n:41)	322.98±72.917	325.00 (214-565)
10th month (n:41)	328.76±93.567	298.00 (219-624)
11th month (n:41)	382.34±140.999	346.00 (192-771)
12th month (n:41)	413.17 ±85.765	342.00 (198-824)
13th month (n:38)	321.42±83.566	298.00 (196-524)
14th month (n:31)	306.94±66.440	286.00 (208-448)
15th month (n:20)	319.40±81.887	298.50 (204-502)
16th month (n:14)	368.57±148.468	353.00 (208-756)
17th month (n:8)	375.50±180.480	286.00 (224-698)
18th month (n:5)	323.40±65.068	312.00 (246-412)
19th month (n:2)	353.00±73.539	353.00 (301-405)
20th month (n:1)	324	324

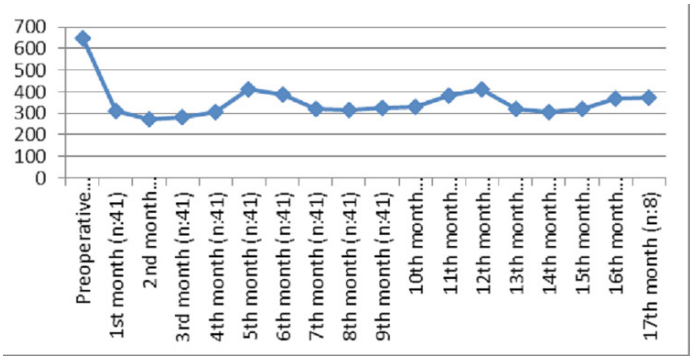

Figure 3. Alterations in CMT of patients during follow-up

DISCUSSION

In this study we reported our clinical results in previously untreated 41 patients with macular edema secondary to RVO who were treated with IDI and we determined that; IDI was highly effective in improving BCVA and CMT with an acceptable increase in IOP levels. During follow-ups, repeated injections were required in most of our patient. Interestingly, on the 1st month follow-up after first injection, the IOP values significantly increased which returned to normal on 2nd month. However, we did not determine significant increases in IOP values after repeated injections. Similarly, BCVA values significantly improved on the 1st month and although there were some alterations through the worse side on 5th-6th and 11th-12th months, these values were still significantly

better than the pretreatment values. The same condition was determined regarding the CMT values. CMT results were significantly better on the 1st month and although there were some alterations on 5th-6th and 11th-12th months, these values were still significantly better than the pretreatment values. On the other hand, complication rates were low in our study. Five (12.2%) patients required medical treatment for increased IOP while 6 (14.6%) patients required surgery for cataract during follow-up period.

The data in literature regarding the outcomes of IDI in RVO were similar with our results. Simsek et al. (8) reported that IDI injections as the first-line treatment resulted in significant improvements in BCVA measurements in 71 RVO patients complicated with macular edema. Niro et al. (9) reported that, in 15 previously untreated CRVO patients complicated with macular edema. BCVA improved significantly with an improvement in retinal sensitivity and central retinal thickness. They concluded that DEX implant led to a significant morphofunctional improvement in treatment naive patients diagnosed with CRVO. Kanra et al. (10) said that in 25 eyes with RVO both mean BCVA and CMT improved significantly with dexamethasone implants alone or in combination with other treatment methods in 18 months follow-up period with very low complication rates. In 6 month follow-up, Li et al. reported that IDI had a favorable safety profile and provided clinically significant benefit in patients with RVO compared with the sham procedure (11). Our results were also compatible with the previous literature that, repeated IDI treatments was safe and effective in RVO- associated macular edema.

In a retrospective study, Blanc et al. (12) reported that repeated IDI injections were an effective treatment for RVO-associated (both branch and central) macular edema in 3 years period in 66 patients with a median age of 72 years. They reported that; the time between injections was 4.8 (4, 2-6) months while cataract progression (70.45%) and increase in IOP (54.54%) were the most commonly seen adverse events. They also reported that they had to continue treatment with anti-VEGF agents in 24.2% patients. The median time to re-treatment was also similar in our study but complication rates were highly lower compared with these results. In another retrospective study on 51 eyes with RVO- associated macular edema, Joshi et al. (13) reported that 56% of patients relapsed after first injection and the median time to relapse was 17 weeks. They reported the rate of significant rise in intraocular pressure as 27% in that study. In our study, all patients required the second injection but the median time was 5 months. In a multicenter, retrospective study in 289 patients with macular edema secondary to RVO who were treated with minimum 2 IDI injections as monotherapy or in combination with other therapies; treatment of macular edema secondary to RVO with minimum 2 IDI injections was determined as effective and safe (14). The re-treatment interval was also approximately 5 months in that study. Although re-treatment is required during follow-up of patients with RVO, 4–5 months intervals are acceptable compared with the injections with anti-VEGF therapies.

Increases in IOP and cataract progression are the most commonly seen adverse effects of ocular corticosteroid treatment (15). Proença et al. (16) analyzed the results of repeated IDI on 18 eyes and reported that, BCVA and CMT improved significantly with this treatment; the mean intervals of re-treatment were 5.1 and 5.4 months, respectively after first and second injections; and IOP elevations were determined in 50% of patients while cataract progression determined in 69% of patients in 17 months follow-up period. However, the complication rates were lower and IOP increases were moderate in severity that was easily managed with medications in our study.

There are some limitations of this study that should be mentioned. First is the low number of patients, since only treatment naive patients were included. Second, we did not compare IDI treatment with other treatment methods, which may be the topic of another study.

CONCLUSION

In conclusion, we determined that, intravitreal dexamethasone injection is an effective mode of treatment in patients with BRVO or CRVO associated macular edema. Its side effects are not severe or common. However the patients should be kept under follow-up for recurrences. Larger, prospective studies are warranted comparing IDI with other treatment modalities in RVO.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports
Ethical approval: Erzincan Binali Yildirim University Clinical Research Ethics Committee (33216249-604.01.02-E.49616).

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