DOI:10.14744/bej.2017.36844
Beyoglu Eye J 2017; 1: 24–28

Original Article

Twelve-month Outcomes of Dexamethasone Implant Treatment in Macular Edema Secondary to Retinal Vein Occlusion in Real Life

Abdullah Ozkaya, Ipek Tanir, Cengiz Alagoz, Zeynep Alkin, Muhittin Taskapili

University of Health Sciences Beyoglu Eye Training and Research Hospital, Istanbul, Turkey

Abstract

Objectives: The aim of this study was to evaluate treatment outcomes of intravitreal dexamethasone implant (IDI) in patients with macular edema (ME) secondary to retinal vein occlusion (RVO), and to assess mean number of visits and injections during 12 months of treatment.

Methods: Records of newly diagnosed RVO patients who were treatment-naïve and had follow-up of at least 12 months were included in this retrospective case series. All patients received initial, single dose of IDI, which was repeated in monthly or bimonthly follow-up when visual acuity decreased by 1 or more lines compared with most recent visit, or an increase in central retinal thickness (CRT) >150 μm was observed in optical coherence tomography images. Primary outcome measures of this study were change in best-corrected visual acuity (BCVA) and CRT. Secondary outcome measures were number of visits and number of injections.

Results: Forty-five eyes of 45 patients were included. Mean BCVA at baseline and month 3, 6, 9, and 12 was 0.15±0.15 decimals, 0.23±0.24 decimals, 0.20±0.20 decimals, 0.18±0.17 decimals, and 0.19±0.20 decimals, respectively. Mean CRT at baseline, and months 3, 6, 9, and 12 was 599±111 μm, 388±137 μm, 421±142 μm, 409±130 μm, and 420±169 μm, respectively. Mean number of planned visits at month 12 was 4.8±1.0, and number of completed visits was 4.2±1.0 (89.0% completion). Mean number of planned injections at month 12 was 1.78±0.7, and number of injections performed was 1.76±0.7 (98.8% completion).

Conclusion: IDI did not appear to be effective agent in real-life conditions of treatment of ME secondary to RVO with respect to visual outcomes. Fact that the study consisted of heterogeneous group of patients, as well as small number of cataract operations and injections were likely main reasons for poor visual outcomes. However, IDI did demonstrate significant effect on anatomical outcomes. Number of both visits and injections was lower than observed in prospective multicenter studies, as expected.

Keywords: Dexamethasone implant, macular edema, retinal vein occlusion.

Introduction

Retinal vein occlusion (RVO) is the second most frequently seen type of retinal vascular disorder after diabetic retinopathy, and macular edema (ME) is most common reason for visual loss in patients with RVO (1–5). Inflammation and increased vascular endothelial growth factor (VEGF) levels both play important role in pathogenesis of ME secondary to RVOs (4–7). Various treatments have been reported to be effective in treatment of ME secondary to RVO (1–8). Currently, intravitreal injections of anti-VEGF agents or steroids are preferred as first-line treatment options for ME (8–10). In the present study, aim was to evaluate outcomes of intravitreal dexamethasone implant (IDI) treat-

Address for correspondence: Abdullah Ozkaya, MD. Beyoglu Goz Egitim ve Arastirma Hastanesi, Bereketzade Cami Sokak, 34421 Beyoglu, Istanbul, Turkey
Phone: +90 212 251 59 00 **E-mail:** abdozkaya@gmail.com

Submitted Date: January 23, 2017 **Accepted Date:** April 12, 2017 **Available Online Date:** May 04, 2017

ment in patients with ME secondary to RVO, as well as to examine mean number of visits and injections administered during first year of treatment.

Methods

This study was retrospective interventional case series. Medical records of patients who had ME secondary to RVO and who underwent IDI treatment between January and December of 2014 were reviewed. Newly diagnosed treatment-naïve RVO patients who had ME <3 months on first admission, and had follow-up of at least 12 months were included. Patients who had co-existing retinal disease (such as diabetic retinopathy or epiretinal membrane), or media opacity that could decrease visual acuity (VA) were not included. Written, informed consent for treatment was obtained from all patients, and the study adhered to tenets of the Declaration of Helsinki.

Data collected from patient records included age, gender, type of RVO, ischemic status, best-corrected visual acuity (BCVA), and central retinal thickness (CRT) at baseline and months 3, 6, 9, and 12, as well as number of visits and number of injections administered.

All patients underwent standardized examination, including measurement of BCVA using Early Treatment Diabetic Retinopathy Study (ETDRS) chart at 4 meters, slit-lamp biomicroscopy and fundus examination, and measurement of intraocular pressure (IOP) via applanation tonometry. Fundus photography, fluorescein angiography (HRA-2; Heidelberg Engineering, Heidelberg, Germany), and optical coherence tomography (OCT) imaging (Spectralis; Heidelberg Engineering, Heidelberg, Germany) were performed before treatment. All examinations were repeated at all visits, with exception of fluorescein angiography, which was repeated only when cause of VA deterioration could not be clarified in clinical examination or with other imaging methods. OCT was used to measure CRT, which was defined as mean thickness of the neurosensory retina in central 1 mm diameter region, and was computed via OCT mapping software provided with device. Fluorescein angiography was inspected for capillary dropout zones at the fovea and peripheral retina, and for leakage, which were accepted as causes of ME. Type of disease was defined as ischemic RVO if ischemic area was ≥5 disc areas in branch retinal vein occlusion (BRVO) patients, or ≥10 disc areas in central retinal vein occlusion (CRVO) patients.

All injections were performed under sterile conditions after application of topical anesthesia, 10% povidone-iodine (Betadine; Purdue Pharma, Stamford, CT, USA) scrub was used on the eyelids and eyelashes, and 5% povidone-iodine was administered to the conjunctival sac. Intravitreal dexamethasone implant (700 μg [mcg]) was injected through the pars plana 3.5 mm posterior to the limbus with 22-gauge preloaded injection system. Patients were called for infection control 2 days after injection and instructed to return to the hospital if they experienced decreased vision, eye pain, or any new symptoms.

Table 1. General characteristics of the patients

Number of eyes	45
Age (years)	63.0±10.4
Gender (male/female)	25/20
Hypertension (%)	31 (68.8)
Diabetes (%)	13 (28.8)
Hyperlipidemia (%)	5 (11.1)
Fluoroscein angiography (non-ischemic/ischemic)	23/22
Type of RVO (BRVO/CRVO)	25/20
Lens status (phakic/pseudophakic)	30/15
Baseline BCVA (decimals)	0.15±0.15
Baseline CRT (μm)	599±111

BCVA: best corrected visual acuity; BRVO: branch retinal vein occlusion; CRT: central retinal thickness; CRVO: central retinal vein occlusion; RVO: retinal vein occlusion.

Initially, all of the patients received single dose IDI injection. Patients were then followed monthly or bimonthly, and single injection of IDI was repeated when VA decreased by 1 or more ETDRS lines from previous visit, or increase >150 μm in CRT was observed in OCT images.

Primary outcome measures of this study were change in BCVA and CRT. Secondary outcome measures were number of visits and injections given.

Statistical Analysis

VA was converted to logarithm of the minimum angle of resolution (LogMAR) for statistical analysis. Categorical variables were presented as numbers and percentages, while numerical variables were expressed as mean and SD. Data were first analyzed in terms of normality using Shapiro-Wilk test. As distribution of the data was determined to be normal, VA and CRT values between baseline and other time points were assessed with repeated measures test. Categorical variables were compared using chi-square test. P value <0.05 was considered statistically significant.

Results

Forty-five eyes of 45 patients were included. Baseline general characteristics are summarized in Table 1. Twenty-five patients (55.6%) demonstrated BRVO, and 20 patients (44.4%) exhibited CRVO. Twenty-three patients (51.1%) had non-ischemic RVO, and 22 patients (48.9%) had ischemic RVO.

Table 2. Mean best corrected visual acuity and central retinal thickness levels at different time points

	Baseline	Month 3	Month 6	Month 9	Month 12
BCVA, decimals	0.15±0.15	0.23±0.24	0.20±0.20	0.18±0.17	0.19±0.20
(LogMAR)	(1.03±0.50)	(0.91±0.54)	(0.94±0.53)	(0.97±0.55)	(0.97±0.54)
CRT, μm	599±111	388±137	421±142	409±130	420±169

BCVA: best-corrected visual acuity; CRT: central retinal thickness; LogMAR: logarithm of minimum angle of resolution.

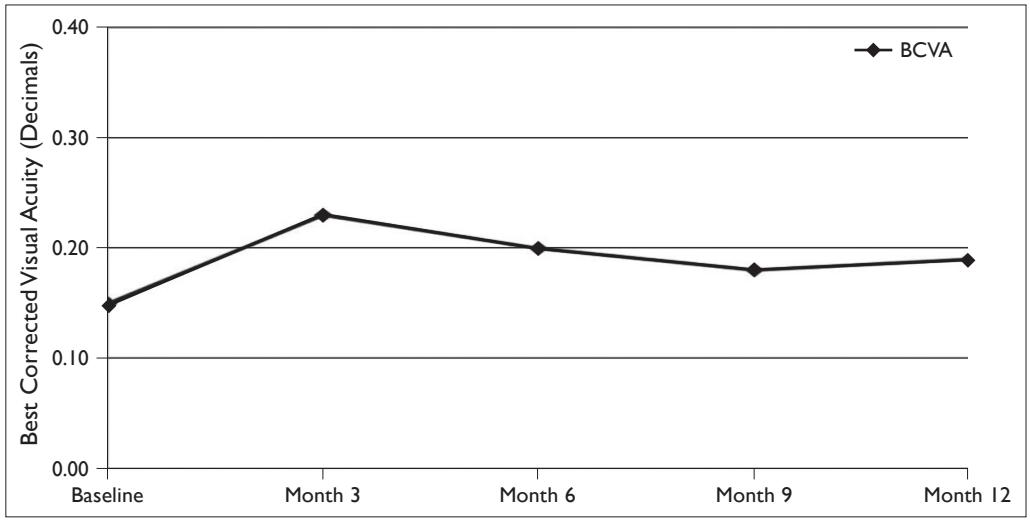

Figure 1. The graph shows change in mean visual acuity level from baseline to month 12.

Mean BCVA at baseline and months 3, 6, 9, and 12 was 0.15±0.15 decimals (range: 0.01–0.5 decimals), 0.23±0.24 decimals (range: 0.01–0.9 decimals), 0.20±0.20 decimals, (range: 0.01–0.7 decimals), 0.18±0.17 decimals (range: 0.01–0.7 decimals), and 0.19±0.20 decimals (range: 0.01–0.7 decimals), respectively (Table 2, Figure 1). With exception of month 3, mean BCVA was not statistically different at any time point compared with mean baseline BCVA (p=0.003 for month 3; p<0.06 for month 6; p=0.2 for month 9; 0=0.3 for month 12). Ten (22.2%) of the 45 patients had gained ≥3 LogMAR lines of VA at month 12. Percentage of patients who had stable VA (lost <3 lines, stable, or gained <3 lines) at month 12 was 64.4% (29/45), and 6 patients (13.3%) lost ≥3 lines of VA.

Mean CRT at baseline and months 3, 6, 9, and 12 was 599±111 μm (range: 413–874 μm), 388±137 μm (range: 226–876 μm), 421±142 μm (range: 201–682 μm), 409±130 μm (range: 207–686 μm), and 420±169 μm (range: 150–987 μm), respectively (Table 2, Figure 2). Mean CRT level was statistically lower than mean baseline BCVA at all time points (p<0.0001 for months 3, 6, 9, and 12).

Mean number of planned visits at month 12 was 4.8±1.0 (range: 2–7), and number of completed visits was 4.2±1.0 (range: 2–7) (89.0% completion). Mean number of planned injections at month 12 was 1.78±1.5 (range: 1–3), and number of injections performed was 1.76±1.4 (range: 1–3) (98.8% completion).

Fourteen patients (31.1%) showed progression in cataract formation during the study period and 2 of them (4.4%) underwent cataract surgery. Nine (20%) of the 45 patients indicated increase >10 mmHg in IOP; however, condition was transient in all cases and treated only with topical antiglaucomatous drops. None of the patients required incisional surgery. No injection-related endophthalmitis was noted after total of 79 injections.

Discussion

In this study, 12 months of real-life outcomes of IDI treatment for ME secondary to RVO were evaluated. VA increased significantly from 0.20 at baseline to 0.23 decimals as early as month 3; however, did not remain significantly better through month 12, as it dropped to 0.20 again in month 6, was 0.18 at month 9, and 0.19 at month 12. CRT level was also found to be significantly lower at months 3, 6, 9, and 12.

In the pivotal prospective multicenter study conducted by Haller et al., efficacy of IDI in treatment of ME secondary to RVO was evaluated (11). Total of 1267 BRVO and CRVO patients were included in the study. Drawback of the research was that second IDI injection was not admin-

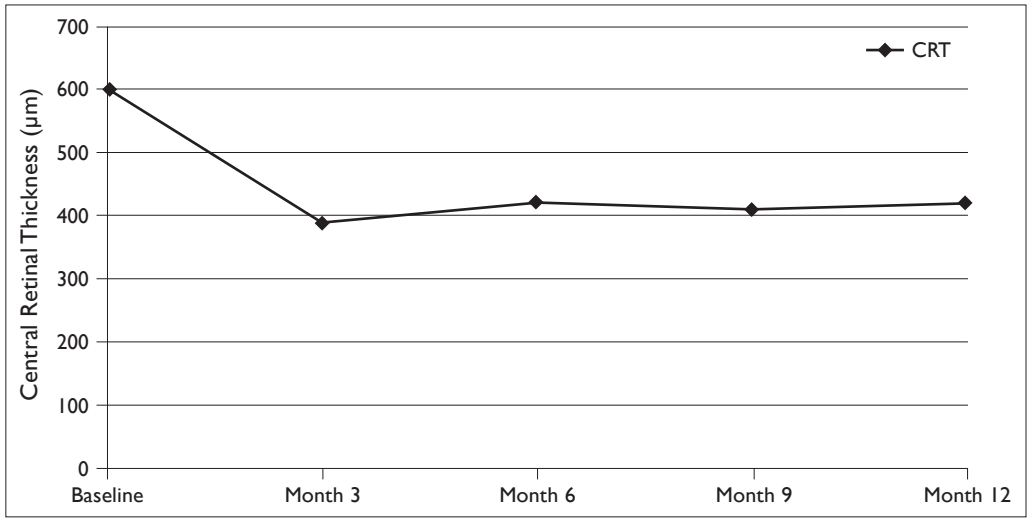

Figure 2. The graph shows change in central retinal thickness from baseline to month 12.

istered for 6 months, and it was detected that efficacy did not last full 6 months. Significant increase in BCVA faded after 2 months. As needed IDI regimens have been followed in treatment of various diseases, and efficacy of single injection has been found to be about 3 to 4 months (12–17). Korobelnik et al. evaluated real-life outcomes of IDI in RVO patients in a multicenter prospective study conducted in France (12). Length of study follow-up was 24 months, and 279 patients were included. Distribution of type of RVO was 53.9% BRVO and 46.1% CRVO. Mean baseline BCVA was 47.7 ETDRS letters and increased by 11.4 letters at week 6 and 4.6 letters at month 24, both of which were statistically significant. However, the included patients were not all treatment-naïve and not all received only IDI treatment. Subgroup of patients who only received IDI monotherapy gained around 5 letters at month 12 and 8.3 letters at month 24. CRT was 554 µm at baseline and decreased significantly to 302 µm significantly at month 24. Another prospective study performed by Eter et al. evaluated relationship between duration of ME associated with RVO and achievement of visual gain in patients treated with IDI (13). The study consisted of 573 patients and mean number of injections was 1.17 during the study period. VA outcomes were better in subgroup of patients with ME duration <90 days than in the patients with duration of >180 days. In a retrospective study conducted by Dugel et al., treatment-naïve RVO patients treated with IDI were reviewed (14). Data of 289 patients who received ≥2 injections were reviewed and 39 treatment-naïve patients were included. After mean follow-up time of 13.9 months and with mean of 2.9 IDI injections, 70.3% of the patients gained ≥3 lines of vision. In that study, 15 of the 39 patients demonstrated IOP >25 mmHg; none required glaucoma surgery. Parodi et al. prospectively evaluated efficacy of IDI treatment in patients with ME secondary to ischemic RVO (15). After follow-up of 12 months, mean baseline BCVA increased from 20/640 to 20/200 in ischemic CRVO subgroup, and increased from 20/125 to 20/63 in ischemic BRVO group. Mean CRT was found to have decreased from 749 µm to 363 µm in ischemic CRVO group, and from 459 to 323 µm in ischemic BRVO group. Mean number of injections was reported to be 2.8 and 2.0 in ischemic CRVO and BRVO groups, respectively. Joshi et al. reported 12-month outcomes of IDI treatment in as needed treatment regimen (16). Retrospectively, 51 eyes of 49 patients were included. They reported that 30% of the eyes gained ≥15 letters of VA and 27% of the patients developed significant rise in IOP. All patients in the study with high IOP responded well to medical treatment; however, 4 eyes with CRVO were reported to show neovascular glaucoma during the study. Mayer et al. prospectively investigated efficacy of IDI in treatment of ME secondary to BRVO and CRVO (17). They added bevacizumab injections to treatment for some of the patients. The supplementary bevacizumab treatment had an additional benefit only in CRVO subgroup. Elevated IOP (>5 mmHg) was detected in 40% of the patients and half of the patients who received 3 IDI injections required cataract surgery. In monotherapy group, mean number of injections was 2.4 for CRVO subgroup and 1.8 for BRVO subgroup, respectively. In combination group, mean number of injections for CRVO and BRVO group was 2.4 and 2.0, respectively.

Our study represents daily practice of our clinic, and so was a retrospective, real-life study. We tried to observe as needed treatment regimen. However, as it was real-life practice, our injection numbers were lower than many previous prospective studies, as well as some previous retrospective studies. Parallel to the low number of treatments, our visual

outcomes were not as good as earlier prospective studies. One-third of the included patients showed progression in their lens opacity; however, only 2 required cataract surgery. One-fifth of our patients experienced increase in IOP >10 mmHg, which was similar to previous reports.

Main limitation of this study was retrospective design. Also, number of included patients was relatively small, though of acceptable size for a study that included only treatment-naïve patients. Furthermore, we evaluated BRVO and CRVO patients together without dividing them into ischemic and non-ischemic subgroups.

In conclusion, dexamethasone implant, which has previously been proven to be effective with regard to visual outcomes in treatment of ME secondary to RVO, might not be satisfactory when patients are undertreated. Mean number of injections was 1.76 over 12-month period in our study, which is lower than previously reported. With this low number of injections, only BCVA remained stable during 12 months and only one-fifth of the patients gained ≥3 lines of vision.

Disclosures

Financial Support: No financial support was received for this submission.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (AO, IT, CA, ZTA, MT); preparation and review of the study (AO, ZTA, MT); data collection (IT, CA); and statistical analysis (AO).

References

1. Scott IU, VanVeldhuisen PC, Oden NL, Ip MS, Blodi BA, Jumper JM, et al; SCORE Study Investigator Group. SCORE Study report 1: baseline associations between central retinal thickness and visual acuity in patients with retinal vein occlusion. Ophthalmology 2009;116:504–12. [CrossRef]
2. Donati S, Barosi P, Bianchi M, Al Oum M, Azzolini C. Combined intravitreal bevacizumab and grid laser photocoagulation for macular edema secondary to branch retinal vein occlusion. Eur J Ophthalmol 2012;22:607–14. [CrossRef]
3. The Branch Vein Occlusion Study Group. Argon laser photocoagulation for macular edema in branch vein occlusion. Am J Ophthalmol 1984;98:271–82. [CrossRef]
4. Augustin AJ, Sahel JA, Cerulli L, Texier-Richard B, Buchholz PM, Kobelt G. Treating retinal vein occlusions in France, Germany, and Italy: an analysis of treatment patterns, resource consumption, and costs. Eur J Ophthalmol 2012;22:776–84. [CrossRef]
5. Bhagat N, Goldberg MF, Gascon P, Bell W, Haberman J, Zarbin MA. Central retinal vein occlusion: review of management. Eur J Ophthalmol 1999;9:165–80.
6. Glacet-Bernard A, Coscas G, Zourdani A, Soubrane G, Souied EH. Steroids and macular edema from retinal vein occlusion. Eur J Ophthalmol 2011;21 Suppl 6:S37–44. [CrossRef]
7. Noma H, Funatsu H, Mimura T, Hori S. Changes of vascular endothelial growth factor after vitrectomy for macular edema secondary to retinal vein occlusion. Eur J Ophthalmol 2008;18:1017–9.
8. Ozkaya A, Celik U, Alkin Z, Faiz Turan M, Yazici AT, Demirok A. Comparison between Intravitreal Triamcinolone with Grid Laser Photocoagulation versus Bevacizumab with Grid Laser Photocoagulation Combinations for Branch Retinal Vein Occlusion. ISRN Ophthalmol 2013;2013:141279. [CrossRef]
9. Yumusak E, Buyuktortop N, Ornek K. Early results of dexamethasone implant, ranibizumab, and triamcinolone in macular edema due to branch retinal vein occlusion. Eur J Ophthalmol 2016;26:54–9. [CrossRef]
10. Ozkaya A, Alkin Z, Yesilkaya C, Erdogan G, Perente I, Taskapili M. Ranibizumab in Macular Edema Secondary to Retinal Vein Occlusion in a Real Life Practice: A Retrospective Case Series. Beyoglu Eye J 2016;1:5–9. [CrossRef]
11. Haller JA, Bandello F, Belfort R Jr, Blumenkranz MS, Gillies M, Heier J, et al; Ozurdex GENEVA Study Group. Dexamethasone intravitreal implant in patients with macular edema related to branch or central retinal vein occlusion twelve-month study results. Ophthalmology 2011;118:2453–60. [CrossRef]
12. Korobelnik JF, Kodjikian L, Delcourt C, Gualino V, Leaback R, Pinchinat S, et al. Two-year, prospective, multicenter study of the use of dexamethasone intravitreal implant for treatment of macular edema secondary to retinal vein occlusion in the clinical setting in France. Graefes Arch Clin Exp Ophthalmol 2016;254:2307–18. [CrossRef]
13. Eter N, Mohr A, Wachtlin J, Feltgen N, Shirlaw A, Leaback R; German Ozurdex in RVO Real World Study Group. Dexamethasone intravitreal implant in retinal vein occlusion: real-life data from a prospective, multicenter clinical trial. Graefes Arch Clin Exp Ophthalmol 2017;255:77–87. [CrossRef]
14. Dugel PU, Capone A Jr, Singer MA, Dreyer RF, Dodwell DG, Roth DB, et al; SHASTA Study Group. Two or more dexamethasone intravitreal implants in treatment-naïve patients with macular edema due to retinal vein occlusion: subgroup analysis of a retrospective chart review study. BMC Ophthalmol 2015;15:118. [CrossRef]
15. Parodi MB, Iacono P, Petruzzi G, Parravano M, Varano M, Bandello F. Dexamethasone implant for macular edema secondary to ischemic retinal vein occlusions. Retina 2015;35:1387–92.
16. Joshi L, Yaganti S, Gemenetzi M, Lightman S, Lindfield D, Liolios V, et al. Dexamethasone implants in retinal vein occlusion: 12-month clinical effectiveness using repeat injections as-needed. Br J Ophthalmol 2013;97:1040–4. [CrossRef]
17. Mayer WJ, Wolf A, Kernt M, Kook D, Kampik A, Ulbig M, et al. Twelve-month experience with Ozurdex for the treatment of macular edema associated with retinal vein occlusion. Eye (Lond) 2013;27:816–22. [CrossRef]