Original Research Article

Effect of intravitreal dexamethasone implant (0.7mg) on intraocular pressure when used for macular edema in real world clinical practice

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Abstract

Aim: To determine the effect of intravitreal dexamethasone implant 0.7mg (Ozurdex; Allergan, Inc.) on Intra ocular pressure when used for macular edema of varying etiology. **Method:** Retrospective non comparative clinical case study of 49 eyes of 49 patients who received a total of 49 injections of intravitreal dexamethasone implant (0.7mg) for macular edema of varying etiology such as diabetes mellitus, vein occlusion, noninfectious uveitis and miscellaneous causes. Best corrected visual acuity, baseline intraocular pressure, status of lens, previous vitrectomy were documented. Intraocular pressure was measured using applanation tonometry on the first, third and sixth month after the injection. All patients were followed up for a period of six months. **Result:** A total of 49 eyes met the inclusion criteria and were analyzed. The cause for macular edema was diabetes mellitus in 22 eyes,(49.9%)) , vein occlusion in 14 (28.6%) uveitis 7(14.3%) and miscellaneous causes in 6 (12.2%) eyes. Mean age of patient was 57 +/- 11.4 (mean +/_ SD) with male 29(59.2%) and female 20 (40.8%). Mean (± SE) BCVA and IOP were 0.62±0.36 log MAR and 14.57±2.5 mmHg, respectively, at baseline and at last follow up at 6 months 0.54+/_0.33 log MAR and 17.29+/_2.4mmHg. Nine (4.4%) patients presented with >5mmHg of increase in IOP from baseline and responded to medical management. No anti glaucoma surgery was performed on any of these patients. There was no progression of cataract and no endophthalmitis reported. **Conclusion:** Nine (4.4%) patients presented with a > 5mmHg in intraocular pressure. In real life clinical practice intravitreal dexamethasone (0.7mg) is a safe option for the treatment of macular edema from various causes.

Keywords: Dexamethasone implant, Intraocular pressure, Macular edema, Visual acuity

Introduction

Macular edema due to various causes remains a primary cause of decreased vision. Diabetic mellitus, vein occlusions, uveitis, are some of the most commonly encountered causes of visual impairment due to macular edema [1]. Advances in investigative modalities with OCT, OCT angiography and improved understanding of intravitreal pharmacokinetics have made a wide armamentarium available to the retina specialist for managing this chronic and complex disorder [2,3].

Lifestyle modification and macular laser have been the standard of care for diabetic macular edema as proposed by the ETDRS Study group [1]. Anti VEGF subsequently has revolutionized management of macular edema [2, 3, 4, 5, 6]. The intravitreal steroids used in the treatment of macular edema are triamcinolone, dexamethasone, fluocinolone, and their anti inflammatory angiostatic and antipermeability effects make them suitable alternatives in the treatment of diabetic macular edema [7].

Intravitreal steroids are indicated as first line treatment options in the following situations - centre-involving DMO in pseudophakics, impending cataract surgery, recent arterial thromboembolic event, previously

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vitrectomized eyes and eyes unresponsive to anti VEGF therapy [8]. Side effects like glaucoma, cataract, and endophthalmitis make them a second line of treatment in comparison to anti VEGF treatment.

Different trials using intravitreal dexamethasone (0.7mg) such as PLACID, MEAD, BEVORDEX have shown intravitreal dexamethasone to have a good safety profile in the management of macular edema due to varying etiologies [9, 10, 11]. This was a retrospective study undertaken to analyze the safety profile of intravitreal dexamethasone implant (0.7mg) – (OZURDEX;Allergan,Inc) in a real world clinical practice. Aim of the study was to determine the rate of glaucoma/ocular hypertension in patients receiving intravitreal dexamethasone 0.7mg for macular edema of varying etiology.

Materials and Methods

49 eyes of 49 patients who received single intravitreal injection of dexamethasone (0.7mg) (ORZURDEX; Allergan, Inc) and with a follow up of six months in a tertiary care teaching hospital in India were retrospectively analyzed. This study was approved by the Research Ethics Committee. Inclusion criteria included patients with central macular edema due to diabetes mellitus, central and branch retinal vein occlusion, posterior non infectious uveitis, age > 18 years, best corrected visual acuity of 0.3 logMAR units or worse, and ability to give informed consent. Steroid responders, those who had previous history of glaucoma and cataract surgery done within 3 months were excluded. Risks of the procedure were explained in detail and informed consent was obtained from all patients. A comprehensive ophthalmic examination including best corrected refractive status, slit lamp examination, intraocular pressure measurement was obtained with applanation tonometry. All patients were subjected to stereoscopic fundus examination after dilation and central macular thickness with OCT was obtained. Previous history of vitrectomy and status of lens was documented. Following the injection of intravitreal dexamethasone (0.7mg) (Ozurdex; Allergan,Inc) patients were examined on first post op day for visual acuity, intraocular pressure and fundus. The same parameters were noted on follow up done at month 1, 3, and 6. Side effects of the injection, if any were also recorded.

Primary outcome measure was visual acuity and intraocular pressure at month 1, 3, and 6 after injection. Mean change in BCVA from baseline to last follow up was calculated, and the mean intraocular pressures at 1, 3 and 6 months were noted and compared to baseline values .An increase in > 5 mmHg from baseline was considered a steroid response. Continuous variables were described as mean and standard deviation. Categorical variables were presented as frequency and percentage.

Data was entered in MS Excel and analysed in SPSS (ver. 20.0). Repeated measures ANOVA and a post hoc test analyses with Bonferroni correction was done to identify significance over 4 measurement of IOP. Wilcoxon Signed Ranks test was applied to find the significance of BCVA measured at baseline and end of follow-up. Any p value less than 0.05 was considered as statistically significant.

Results

Table-1: Demographics and Baseline characteristics of patient

Characteristics	DMO (n=22)	RVO (n=14)	UVEITIS (n=7)	All patients (n=49)
Age (mean±SD)	58.8 ± 10.3	59.6 ± 9.5	54.6 ± 13.4	57.0 ± 11.5
Sex				
Male (n, %)	19 (86.4)	6 (42.9)	3 (42.9)	29 (59.2)
Female (n, %)	3 (13.6)	8 (57.1)	4 (57.1)	20 (40.8)
DM (n, %)	22 (100.0)	7 (50.0)	1 (14.3)	30 (61.2)
Previous injection (n, %)	10 (45.5)	8 (57.1)	2 (28.6)	22 (44.9)
VIT (n, %)	2 (9.1)	0 (0.0)	2 (28.6)	5 (10.2)
Lens				
Phakia (n, %)	9 (40.9)	(6 (42.9)	5 (71.4)	25 (51.0)
Pseudophakia (n, %)	13 (59.1)	8 (57.1)	2 (28.6)	24 (49.0)

Note: Percentages are within group

A total of 49 eyes met the inclusion criteria and were analysed. There were 29 (59.2%) male and 20 (40.8%) female. Mean age of patient was 57.0 ± 11.5. The causes for macular edema were diabetes in 22 eyes (44.9%), vein occlusion in 14 (28.6%), uveitis in 7 (14.3%) and miscellaneous causes in 6 (12.2%) eyes. 22 eyes had received a previous injection of either ranibizumab (n=18) or dexamethasone implant (n=4). Twenty five (51%) of eyes were phakic and 24(49%) pseudophakic (Table 1). Of the 49 eyes 5 (10.2%) eyes had a previous history of vitrectomy. A total of 9(4.4%) of patients has an elevation >5mmHg from baseline during the six month follow up period.

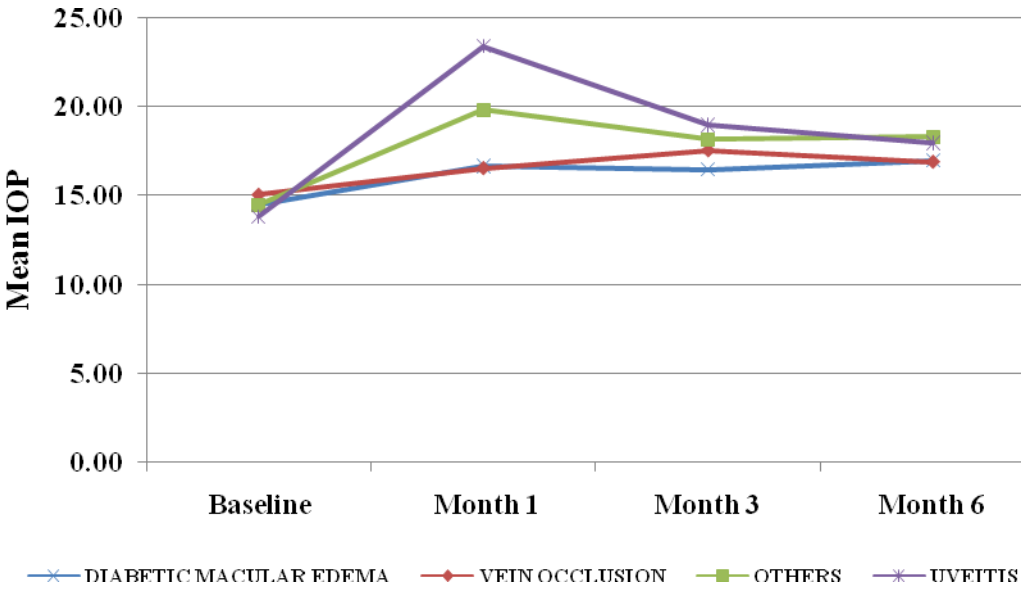

Figure-1: Mean IOP at various time points according to different conditions of the patient.

Mean (± SD) of BCVA, and IOP were 0.622 ± 0.4 logMAR and 14.57 ± 2.5 mmHg, respectively, at baseline and at last follow up at 6 months 0.541 ± 0.3 logMAR and 17.29 ± 2.5 mmHg.

The mean and SD at various time points according to different conditions of the patient were given in Table 2 for IOP and in Table 3 for BCVA. Repeated measures ANOVA with Greenhouse-Geisser correction showed [$F_{(1.9, 86.1)}$ =15.0; $p < 0.001$] significant difference over the month in IOP. However the difference in IOP at the end of 6 months between groups is not statistically significant ($p = 0.253$).

A post hoc analyses with Bonferroni correction showed there is statistically significant difference only in DMO group between baseline and at 6 months ($p = 0.01$). The peak IOP in patients with uveitis, diabetic macular edema and vein occlusion was at 1 month after the dexamethasone implant. There was no difference in the amount of pressure elevation in patients with macula odema due to diabetis and vein occlusion at 1 month (Figure 1). All patients responded to treatment with anti glaucoma medications and IOP was normal on last follow up at 6 months.

Table-2: Mean and standard deviation (SD) of IOP at various time points according to different conditions of the patient.

Conditions	Baseline	Month 1	Month 3	Month 6
DMO	14.5 ± 2.7	16.7 ± 5.2	16.5 ± 3.0	17.0 ± 2.6
RVO	15.1 ± 2.5	16.6 ± 6.4	17.6 ± 5.1	16.9 ± 2.8
Uveitis	13.9 ± 2.1	23.4 ± 7.0	19.0 ± 4.9	18.0 ± 2.4

Table-3: Mean and standard deviation (SD) of BCVA at two time points according to different conditions of the patient.

Conditions	BCVA at Baseline	BCVA at Month 6
DMO	0.694 ± 0.4	0.659 ± 0.4
RVO	0.546 ± 0.3	0.486 ± 0.3
Uveitis	0.750 ± 0.3	0.464 ± 0.1

Table-4: BCVA at baseline and at 6 months

	BCVA at Month 6		
BCVA at Baseline	**Conditions**	≤ 1	> 1
	≤ 1	43	0
	> 1	3	3

IOP-lowering medication was initiated in all patients with IOP >21mmHg, Glaucoma surgery was performed in none of all study eyes. There was no cataract progression and endophthalmitis was not reported in the 6 month follow up period.

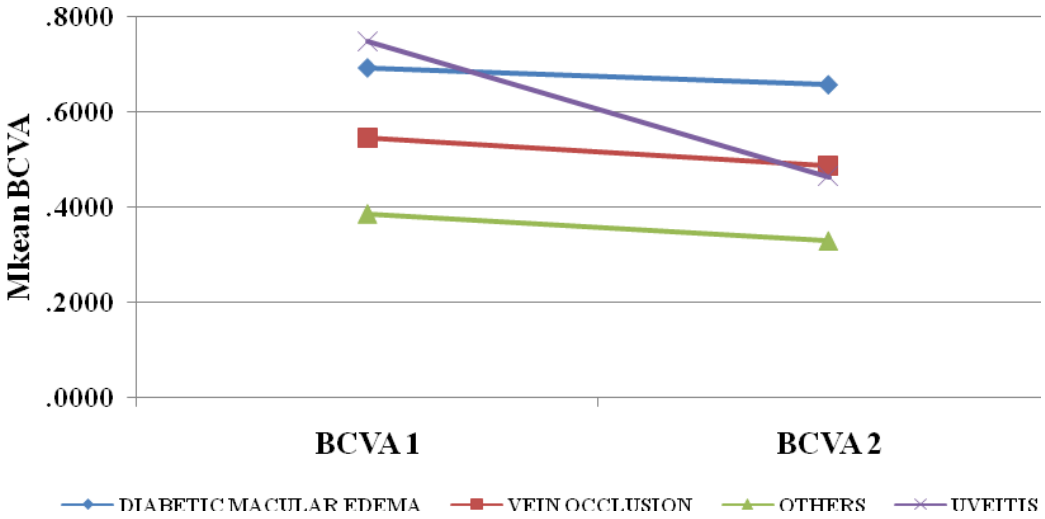

Figure-2: Mean BCVA at baseline and at end of 6 month according to different conditions of the patient.

Table 4 compares BCVA measured at baseline and at after 6 month. All the patients (43; 100%) whose BCVA less than or equal to 1 logMAR unit at baseline remained less than or equal to one at after 6 month. Out of 6 patients whose BCVA more than 1 logMAR unit at baseline, improvement to less than or equal to 1 logMAR unit was seen after 6 month in 3 (50%) patients. Out of these 3 patients two were DMO and one Uveitis. Overall as well as within each underlying conditions there is no statistically significant difference between BCVA baseline and at after 6 month. However there was an improvement in BCVA among uveitis patients (Figure 2).

Discussion

We report our experience on the rate of glaucoma /ocular hypertension in a retrospective analysis of 49 eyes who received intravitreal dexamethasone (0.7mg) for macular edema from varying etiologies-diabetic macular Edema, retinal vein occlusion, uveitis, and miscellaneous causes. Simiar results from different populations have been published. A retrospective study The Chrome Study [12] reported the greatest mean peak changes in BCVA lines of vision occurred in study eyes with uveitis (3.30.6, *P0.0001),* followed by RVO (1.30.5, *P0.01)* and DME (0.70.5, *P0.05*),.Our study showed a similar improvement in visual acuity in eyes with macular edema due to uveitis, in comparison to macular edema due to diabetes and vein occlusion. A similar retrospective study was conducted in patients with BRVO-related or CRVO related ME (n289) who

received two or more DEX implant injections. The patients received a mean of 3.2 (range 2–9) DEX implant injections, alone or combined with other therapies and a subsequent improvement in visual acuity was noted [13]. A retrospective study in Germany on 102 patients noted a significant improvement in BCVA following a single Injection of dexamethasone [14]. Yet another retrospective study on macular edema secondary to uveitis on 38 eyes improved ocular function was observed following intravitreal dexamethasone injection [15]. Two large randomized sham controlled phase 3 trails have reported the safety and efficacy intravitreal dexamethasone in the management of diabetic macular edema [9]. In both studies, rates of glaucoma surgery were low (0% in CHROME study DME eyes; 1.4% in MEAD study eyes), and the proportion of study eyes with increased IOP (IOP change 10 mmHg, absolute IOPs 25 mmHg or 35 mmHg) was similar. The most common adverse effect was increase in intraocular pressure in our study 9 (4.4%) which is lesser than that reported by other studies. The Chrome study reported an increase in intraocular pressure in 20.8% of patients and 17.5% of eyes required IOP lowering medication [12]. The results of Phase III trials of the DEX implant concluded by the end of the study period, no more than 24% of RVO and 23% of uveitis study eyes required use of IOP-lowering medications [16,17]. Almost all eyes with increased intraocular pressure were managed with one or two IOP lowering medications. There were no cataract or glaucoma surgeries performed in any of the eyes during the course of the study.

Conclusion

Anti VEGF agents remain the first line in the management of macular edema. However eyes that are nonresponsive to anti VEGF, with the burden of repeated injections, eyes with center involving macular edema, pseudophakics, those with impeding cataract surgery, recent thromboembolic events or vitrectomized eyes are suitable candidates where intravitreal dexamethasone implant can be used alone or in combination with anti VEGF agents. The safety profile with a low rate of glaucoma /ocular hypertension makes intravitreal dexamethasone implant a suitable and safer alternative to earlier steroids that had a greater propensity to cause an increase in intraocular pressure.

A major limitation of this study is the retrospective nature. Prospective randomized trials will further shed light on the emerging role, safety and efficacy of intravitreal dexamethasone implant (0.35mg, 0.7mg) in the management of macular edema of varying etiology.

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