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Original Article

Visual and Anatomical Outcome Of Ozurdex Implant In Non-Infectious Intermediate Or Posterior Uveitis In Treatment Naive Patients

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Abstract

Aim:- *To determine the visual and anatomical outcome of Ozurdex implant in non-infectious intermediate or posterior uveitis in treatment naïve patients.*

Design:- *Retrospective study.*

Materials and Methods:- *25 eyes receiving Ozurdex implant (0.7mg dexamethasone) for treatment of naïve non-infectious intermediate or posterior uveitis with cystoid macular edema (CME) having a minimum 6 month follow up. Best corrected visual acuity (BCVA) and central foveal thickness (CFT) was measured at baseline, 1, 3 & 6 months.*

Results:- *Mean baseline logMAR BCVA improved significantly from 0.477 to 0.181 ($p<0.05$) at 3 months and to 0.193 ($p<0.05$) at 6 months. The mean CFT reduced from its baseline value of 481.3µ to 250.41µ ($p<0.05$) at 3 months and to 274.8µ($p<0.05$) at 6 months.*

Conclusion:- *Significant improvement in BCVA and CFT from baseline to 3 and 6 months has proven Ozurdex implant to be a promising treatment option in cases of treatment naïve non-infectious posterior uveitis.*

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Keywords: *Ozurdex implant, intermediate, posterior uveitis*

Introduction

Uveitis is a common ocular pathology with an annual incidence of approximately 17-52 cases per 100 000 and prevalence of 38-714 per 100 000.[1] It can be classified anatomically into anterior, intermediate, posterior and panuveitis. Uveitis can also be divided based on its aetiology into infectious, non-infectious, and masquerade syndromes (neoplastic and drug-induced). The course of uveitis may be defined as acute, recurrent or chronic.

Intermediate uveitis and posterior uveitis affect the posterior segment of the eye and are often unresponsive to topical administration of steroids due to less than optimum therapeutic drug penetration beyond the lens. Periocular and subtenon steroids could be effective in treating some patients with uveitis associated cystoid macular edema (CME) but these are associated with higher incidence of complications like cataract, glaucoma, ptosis, globe perforation etc. Long-term systemic corticosteroid therapy is required in patients with an associated systemic disease and in those with bilateral ocular inflammation. Although effective, it is associated with a variety of potentially serious adverse effects such as induction or worsening of hypertension and diabetes mellitus, osteoporosis, and adrenal suppression.

Macular edema (ME) has been reported to occur in one third of cases of posterior uveitis, which is most often termed as 'uveitic macular edema'.[2] It is due to breakdown of blood retinal barrier and leakage of contents in and around the macula. Ozurdex is a biodegradable intravitreal dexamethasone implant approved by the United States Food and Drug Administration for treatment of macular edema associated with vein occlusion, diabetic retinopathy and for treatment of noninfectious posterior uveitis. The effective use of Ozurdex implant in treatment naïve patients with non infectious posterior and intermediate uveitis has not been shown in any previous studies to the best of our knowledge. In this study, we report our experience with dexamethasone implant in this subset of patients with 6 months follow up.

Material And Methods

This is a single centre, retrospective study of 25 eyes of 22 patients, who were diagnosed with non infectious posterior uveitis (Pars planitis, vasculitis, choroiditis, Vogt Koyanagi Harada with cystoid macular edema and/or Vitritis), in the uvea clinic of a tertiary care centre. Patients who did not receive any treatment earlier, were recruited in the study from January 2014 to January 2016, after obtaining an informed consent. All patients underwent investigations like Complete blood count, Erythrocyte sedimentation rate, Montoux, chest X ray, RA factor, Toxo titres (IgG and IgM) and TPHA to rule out any possibility of infection.Patients who had macular edema due to any cause other than non-infectious posterior uveitis were excluded (e.g., diabetes ,vein occlusion and Irvine Gass Syndrome). Treatment protocol included intra-vitreal injection of Ozurdex implant (700 µg, Allergan, Inc., Irvine, CA), administered in accordance with the manufacturer's guidelines using the 22-gauge applicator device under aseptic conditions in the operation theatre and with oral steroids (as and when required). The patients were then followed up and the outcomes were analyzed at 1, 3 months and 6 months for best-corrected visual acuity (BCVA) using Snellen visual acuity charts converted to logarithm of the minimum

Table 1: Comparison of outcome pre and post Ozurdex implant

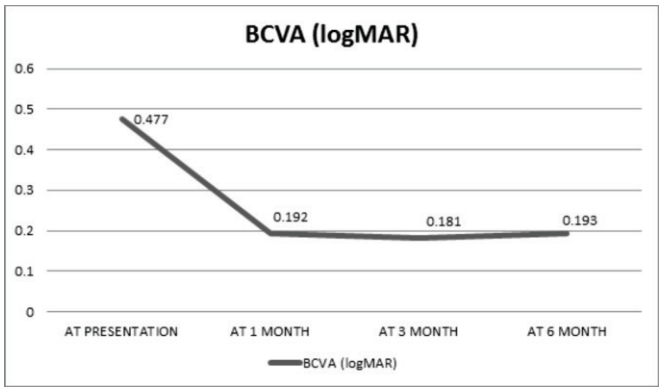
Patient	Age Of Patient	Baseline Bcva	Bcva At 1 Month	Bcva 3 Months	Bcva 6 Months	Baseline Cft	Cft At 1 Month	Cft 3 Months	Cft 6 Months
Pars Planitis									
1	43	0.6	0.17	0.17	0.17	602	228	248	352
2	50	0.6	0.6	0.17	0.17	498	337	272	308
3	48	0.3	0.3	0.3	0.3	207	210	228	308
4	23	0.3	0.17	0.17	0.17	888	316	296	344
5	38	0.77	0	0	0.17	638	236	256	322
6	54	0.3	0	0	0	575	228	256	258
7	35	0.47	0.3	0.3	0.3	319	228	240	264
8	10	0.47	0	0	0	542	239	248	302
9	10	0.3	0.17	0.17	0.3	412	255	266	289
10	56	0.47	0	0	0	798	194	208	210
11	56	1.301	1	1	1	619	155	186	192
12	56	0.17	0.17	0	0	323	260	278	277
13	46	0.47	0.17	0.17	0.17	548	229	240	257
14	41	0.3	0.17	0.17	0.17	731	250	265	333
15	55	0.6	0.17	0.17	0.17	247	191	191	190
Vasculitis									
16	60	0.6	0.17	0.47	0.47	403	205	258	268
17	23	0	0	0	0	220	224	224	232
18	44	0.3	0.3	0.3	0.3	225	207	210	210
19	56	0.3	0.17	0.17	0.17	280	235	244	274
20	20	0.47	0.17	0.17	0.3	518	351	340	366
21	52	0.47	0	0	0	555	262	260	296
22	52	0.3	0	0	0	378	234	232	278
23	31	0	0	0	0	370	216	279	275
Chorioditis									
24	62	0.3	0.3	0.3	0.3	260	246	246	242
VKH									
25	32	1.301	0.3	0.3	0.3	877	333	280	308

angle of resolution (logMAR) units for statistical purpose, and central foveal thickness (CFT) measured by Spectral domain optical coherence tomography (SD-OCT, Spectralis, Heidelberg Engineering Inc., Heidelberg, Germany). An increase in CFT by > 50μ from the baseline was considered significant and decrease in BCVA by more than 10 letters was considered significant in our study. Data analysis was done with the help of a computer using SPSS version 22.0. Paired t-test was used to test the significance of difference between quantitative variables. A $P < 0.05$ is taken to denote significant relationship.

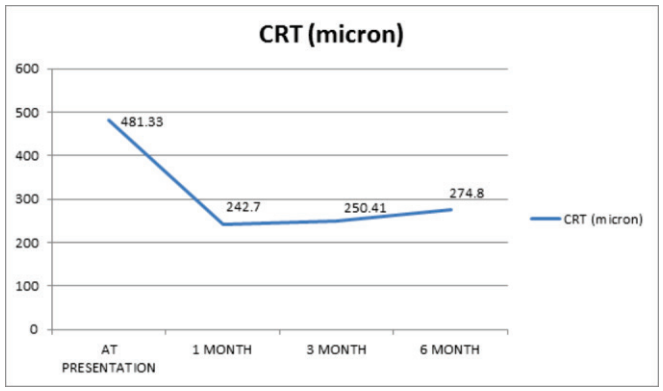
Results

A total of 25 eyes of 22 patients were included in the study with varying etiologies of intermediate and posterior uveitis. 15 patients with pars planitis,[8] patients with vasculitis and 1 patient of each VKH & choroiditis were included. There were equal percentage of males and females in our study. The mean age group of patients who received Ozurdex implant during the study period was 40.4 years (range 10-56years). All cases and their change in best visual corrected vision (BCVA) and central foveal thickness (CFT) pre and post Ozurdex implant is depicted in detail in Table 1. The mean baseline visual acuity improved from logMAR0.477to0.192 and 0.181 at 1 and 3 months respectively. Later at 6 months

it dropped to 0.193 logMAR units [Graph 1].
The mean CRT improved from 481.3 to 242.7 and 250.41 from baseline to 1 and 3 months. But it increased further to 274.8 at 6 months post implant [Graph 2].
One eye required cataract surgery within 6 months period after the implant. Three eyes developed intraocular pressure (IOP) >21 mmHg at 1 month follow-up post implant. All eyes were medically managed for raised intraocular pressure. None of the eyes required anti glaucoma surgery. 2 patients previously diagnosed pars planitis had recurrence of macular edema at 3 months and were advised for reinjection during the study period.



Graph 1: *Change in BCVA (in LogMAR) at presentation, 1, 3 and 6 months*



Graph 2: *Change in mean CRT at 1, 3 and 6 months from baseline*

Discussion

The Ozurdex implant delivers dexamethasone in a sustained-release fashion over several months, the drug concentrations decrease over time. Chang-Lin et al described the pharmacokinetics of Ozurdex in animal models. They described a 2-phase drug release after implantation, with the highest retinal concentrations observed in the first 60 days, followed by a second phase in which much lower concentrations of DEX were released.[4]
In our study there was a statistically significant improvement in BCVA at 1, 3 and 6 months from the baseline. But there was no statistically significant improvement in visual acuity from 3 months to 6 months (Graph 1). Palla et al studied 20 eyes of 15 patients and noticed BCVA had improved at 6 weeks and also on second follow up but the improvement was not statistically significant at second follow up. To development of cataract.[3] In our study only one patient developed significant cataract during 6 month follow up requiring cataract surgery. A study by Zarranz-Ventura et al has also shown improvement of BCVA at their 1 month follow-up.[5] HURON study group showed more improvement from baseline BCVA in Ozurdex implant group.[6] The mean CRT in our study showed statistically significant improvement at 1and 3 months compared to the baseline, which was maintained up to our last follow-up at 6 months though maximum improvement had occurred in the first 3 months of the implant (Graph 2). In the study by Cao et al for persistent uveitic macular edema, there was statistically significant reduction in mean CRT at 1 month and improvement in visual acuity at 3 months, the mean time to recurrence of CME was 4.6 months.[7] Palla et al found statistically significant improvement in mean CFT at 6 weeks post implant.[3] Myung et al also reported good outcomes of dexamethasone implantation to control intraocular inflammation in non-infectious posterior uveitis patients with effect lasting 3-4 months.[8]
In our study 3 eyes (12%) developed raised IOP , which were successfully managed with antiglaucoma medications. No patients in our study required antiglaucoma surgery. 23% of the eyes in HURON study and 15% in the study by Palla

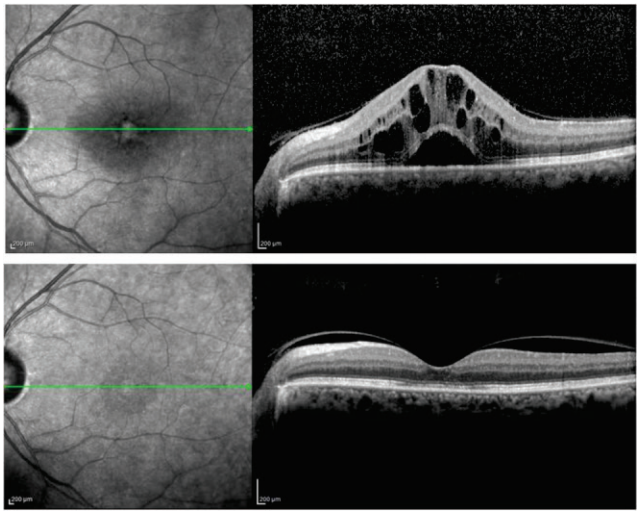


Figure 1: *Optical Coherence Tomography showing lost foveal contour and diffuse thickening of the retinal layers and lack of differentiation of retinal layers suggesting ischemia*

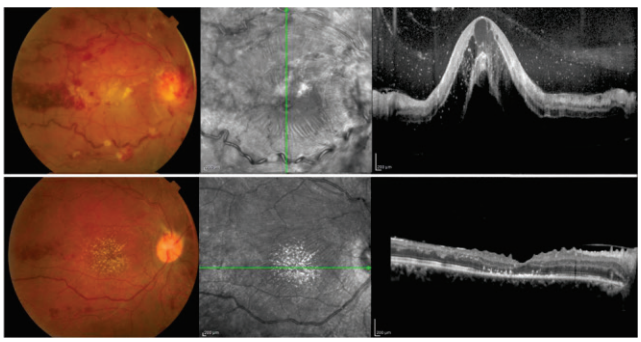


Figure 2: *Pre and 3 months post injection Fundus and OCT images of a case of vasculitis*

et al needed antiglaucomatreatment.

Two eyes (8%) of our patients showed recurrence of macular edema during the study period and were advised reinjection. Zarranz-ventura et al observed 51% reinjection frequency; the second injection was performed approximately 6 months after the initial one.[5] One of the limitation of our study is the short duration follow up of 6 months, a longer follow-up is required to see the recurrence rate and need for reinjection. Yap et al showed 2 of the 6 eyes had recurrences and required reinjection.[11] No other complications like endophthalmitis, vitreous hemorrhage and retinal Ozurdex detachment were observed in our study.

To the best of our knowledge this is the only study on treatment naïve patients looking for change in BCVA and CFT after Ozurdex implant in cases with intermediate or posterior uveitis. The main limitations of this study are that it has a retrospective study design with a mean follow up of 6 months post Ozurdex impant. The study cohort was small to comment, especially with respect to its effect on consistent maintenance of the CFT and cataract (cataracts may take longer than 6 months to develop). Oral steroids were also supplemented along with the implant, so the duration and efficacy of only implant could not be studied.

From the results the analysed with improvement in vision and decrease in macular thickness we advocate the use of dexamethasone implant in treatment naïve patients with non-infectious posterior uveitis. twenty of 22 patients are on further follow up. The frequency of recurrences and development of complications in the follow up period may help us in improving the management in these eyes.

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