

## Outcomes of Intravitreal Dexamethasone Implant in Persistent Macular Edema Due to Retinal Vascular Diseases

### Intravitreal Dexamethasone Implant in Persistent Macular Edema

\*Arunava kundu<sup>1</sup>, Debabrata datta<sup>2</sup>, Sneha batra<sup>3</sup>, Aniket ginodia<sup>3</sup>, Preeyam biswas<sup>4</sup>, Partha biswas<sup>5</sup>

<sup>1</sup>Associate Professor, Esipgimsr & Esic Medical College, Joka, Kolkata;

<sup>2</sup>Associate Professor, Icare Medical College, Haldia;

<sup>3</sup>Fellow, B B Eye Foundation, Kolkata;

<sup>4</sup>Ms Student, Dr. D Y Patil Medical College, Hospital & Research Centre, Pune;

<sup>5</sup>Director, B B Eye Foundation, Kolkata

Corresponding Author: Sneha Batra

#### Abstract:

**Purpose:** To evaluate the safety and efficacy of intravitreal Dexamethasone implant in patients with persistent macular edema due to retinal vascular diseases.

**Methods:** This retrospective analysis was done after intravitreal injections of 0.7mg Dexamethasone implant Ozurdex in 22 eyes of 21 patients with persistent macular edema due to retinal vascular diseases either after at least one anti-VEGF intravitreal injection or photocoagulation from April 2015 to March 2016. Best corrected visual acuity (BCVA) was assessed through Snellen's chart, and converted to logMar scale. Central macular thickness (CMT) was measured by Spectral-Domain Optical Coherence Tomography (SD-OCT). BCVA, Intraocular pressure (IOP) and CMT was noted at baseline (M0) and repeated after one month, three months, four months, and six months post injection.

**Results:** The average thickness of the retina at baseline was 652 $\mu$ m, the median BCVA was 0.8 logMAR, and corrected intraocular pressure was 12.8 mmHg. The maximum decrease in mean retinal thickness was observed at four weeks following the treatment and was 298 $\mu$ m, and visual acuity improved by an average of four lines and was 0.4logMAR. No complications were observed during the follow-up.

**Conclusion:** Intravitreal Dexamethasone implant appears effective in management of persistent macular edema due to retinal vascular disease with high safety level.

**Keywords:** Dexamethasone implant, Ozurdex, macular edema, intravitreal steroid

**Summary:** Retrospective analysis was done in 22 eyes of 21 patients with persistent macular edema due after implantation of intravitreal Dexamethasone implant

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### I. Introduction

Retinal vascular diseases are one of the most devastating diseases, which affect the retina both structurally and functionally. In day to day clinical practice, most common retinal vascular diseases are diabetic retinopathy, branch retinal vein occlusion, central retinal vein occlusion and arterial occlusion. In case of retinal vein occlusion or diabetic retinopathy, macular edema is the most common cause of reduced visual acuity. Diabetic macular edema (DME) is currently one of the most common causes of decreased visual acuity in the working population. DME can be either ischemic or exudative, based on the dominant underlying disease mechanism. In ischemic DME, the pathology is a reduction in blood flow to the macula which causes reduced central vision and swelling of the retinal tissues in this area. In exudative DME, excessive leakage of fluid from the blood vessels around the macula results in thickening or swelling of the retina and a resultant reduction in central vision. In a patient with DME, it is usually a combination of both these patho-mechanisms.

Vascular endothelial growth factor (VEGF) has been implicated as a potential cause of vascular abnormalities seen in diabetic macular edema<sup>1</sup>. Corticosteroids have been shown to inhibit the expression of VEGF. Additionally, corticosteroids prevent the release of prostaglandins, some of which have been identified as mediators of cystoid macular edema. Intravitreal injections of triamcinolone acetonide have produced

benefits in patients with DME<sup>2</sup>, but several adverse events like high intraocular pressures and cataract have been reported, which have limited its use<sup>3</sup>.

Dexamethasone, a potent corticosteroid, has been shown to suppress inflammation by inhibiting release of prostaglandins, preventing fibrin deposition, capillary leakage, and phagocytic migration of the inflammatory response<sup>4</sup>. By delivering a drug directly into the vitreous cavity, the blood-eye barriers are circumvented and intraocular therapeutic levels can be achieved with minimal risk of systemic toxicity. This route of administration typically results in a short half-life unless the drug can be delivered using a formulation capable of providing sustained release. Dexamethasone Posterior-Segment Drug Delivery System is composed of biodegradable copolymer containing micronized dexamethasone. The drug-copolymer complex gradually releases the total dose of dexamethasone over a series of several months after insertion into the vitreous with minimum complications and optimum results. The purpose of our study was to evaluate the safety and efficacy of intravitreal Dexamethasone implant in patients with persistent macular edema due to retinal vascular diseases

## **II. Methods**

In this retrospective, interventional series, 22 eyes of 21 patients with DME or persistent macular edema from branch retinal vein occlusion or central retinal vein occlusion, for a period ranging from 4-12 months were studied. Inclusion criteria included patients with persistent macular edema due to diabetes or other vascular occlusion, who have the following criteria: age older than 18 years, BCVA of 0.3 logMAR units or worse, persistent macular edema involving the center of the fovea 3 or more months after one or more treatment of focal macular laser photocoagulation and/or intravitreal anti-VEGF injections. Exclusion criteria included a history of corticosteroid-responsive intraocular pressure (IOP) rise, cataract extraction or other intraocular surgery within 3 months and any other laser treatment in last 1 month (including Nd:YAG laser capsulotomy). After a detailed explanation of the risks and benefits of the injection and obtaining written informed consent, a comprehensive ophthalmic history was elicited from all patients. Clinical examination included best-corrected Snellen visual acuity, IOP measurement, anterior segment examination including evaluation of lens status, dilated fundus examination and Optical Coherence Tomography (OCT) of the central macula showing thickness at baseline. Patients underwent Ozurdex implant in operating room under topical anesthesia. All patients received topical Moxifloxacin 0.3% eye drops six times/day for 3 days prior to and 5 days post-injection and were examined on day 1 for visual acuity, anterior chamber reaction, IOP and fundus examination.

The recommended technique for intraocular injection of the implant is described. The patient is prepared in operating room with the same standards as followed for intraocular procedures. Maintaining aseptic technique, the cap is carefully removed from the applicator. The safety tab is pulled straight off the applicator without twisting or flexing it. The long axis of applicator is held parallel to limbus and sclera is engaged at an oblique angle with bevel of the needle up to create a shelved scleral path, 4 mm away from limbus. The needle-tip is advanced within the sclera for about 1 mm, and then redirected towards the center of the eye and advanced until the penetration of sclera is completed and vitreous cavity is entered. The needle should not be advanced past the point where the sleeve touches the conjunctiva. The actuator button is slowly depressed until an audible click is noted. Before withdrawing the applicator from the eye, one makes sure that the actuator button is fully depressed and has locked flush with the applicator surface. The needle is removed in the same direction as while entering the vitreous cavity. Fundus is carefully examined.

All patients were examined on post-operative day 1 for visual acuity, anterior chamber reaction, intraocular pressure (IOP), and fundus evaluation by indirect ophthalmoscopy. Complete ocular examination and OCT was performed at periodic intervals, thereafter. The main outcome measure was visual acuity at 1, 4 and 6 months after injection. Secondary outcome measures included change in central macular thickness on OCT, changes in IOP, and development of any side effects resulting from the intravitreal injection of the Dexamethasone implant. Out of 22 eyes (21 patients) with persistent macular edema that underwent the implant, six eyes had follow-up of more than 6 months post-injection. The mean age of the patients was 54 years (range 42-64 years).

## **III. Results**

Diabetic retinopathy was the most prominent (79% cases) cause of persistent macular edema followed by central retinal vein occlusion (14%) and branch retinal vein occlusion (7%). (Fig – 1) All cases had received treatment since 3 months prior to the Dexamethasone implantation. Most of the patients received intravitreal anti-VEGF injection followed by laser therapy according to the disease. Pretreatment history is shown in Table 1. The mean baseline IOP was 16 mmHg (range 12-20 mm Hg). 12 eyes were pseudophakic whereas others were phakic with nuclear sclerosis. The last follow-up was up till 6 months following Ozurdex implant. Preoperative mean CMT was 652  $\mu$ m (Range 525 – 936  $\mu$ m) which improved to 298  $\mu$ m (Range 175 to 315  $\mu$ m) at month 1 and increased to 495 microns at month 4. (Fig-2).

Preoperative mean BCVA was 0.6 logMAR units which improved to 0.2 logMAR units at month 1 and 0.4 logMAR units at month 3. (Fig – 3) No clinically significant rise of IOP occurred in any of the eyes. None of eyes showed progression of cataract from the baseline.

#### **IV. Discussion**

Management of persistent macular edema which is refractory to laser photocoagulation, anti-VEGF injections or intravitreal triamcinolone acetonide (IVTA) is challenging and the treatment options are limited. The recent randomized, controlled trials have shown that laser photocoagulation, intravitreal injections of anti VEGF agent Ranibizumab and corticosteroid triamcinolone acetonide have been useful in treatment of macular edema. These studies also show, however, that repeated treatments are often required to control macula edema, prevent vision loss, and increase the chance of visual improvement.

Multiple recent studies<sup>5-7</sup> in eyes with persistent macular edema demonstrated that Dexamethasone implant produced improvement in visual acuity, macular thickness, and fluorescein leakage that were sustained for up to 6 months. The study included eyes with macular edema due to a variety of causes, including diabetic retinopathy, retinal vein occlusion<sup>8</sup>. A subgroup analysis of the key efficacy findings for eyes with different causes of macular edema found that the results for each group were generally consistent with those for the entire study population. In our study, it was seen that there is significant reduction in CMT compared to baseline levels at month 1. The maximum reduction in macular thickness was seen at month 1 followed by re-appearance of macular edema at month 4. This showed that the peak effect of the drug was in between 1 and 4 months, which is significantly different compared to eyes with macular edema secondary to CRVO or BRVO where the drug effects lasts for 6 months as reported in other studies.

The mean post-injection BCVA at month 1 showed improvement in all eyes but was not as significant as the reduction in CMT at the same timeline. This could be explained by the fact that these eyes had chronic, recalcitrant macular edema and diabetes mellitus since more than 15 years which could have led to irreversible changes in the macula. Rise in IOP is a known side effect after intraocular corticosteroid injections<sup>9</sup>. In our study, none of the eyes had a significant rise of IOP. Studies have shown that percentage of eyes receiving triamcinolone (4 mg) have higher risks of IOP elevation more than or equal to 10 mm Hg (8.9%) compared to sustained release of Dexamethasone (0.9%) in patients with macular edema secondary to RVO over the course of 12 months. None of the eyes had significant cataract progression which could have caused significant reduction in visual acuity at 4 months compared to baseline level. Since the effect of the Dexamethasone implant appears transient, repeated injections may be necessary to maintain visual improvement. Whether repeat injections will result in same amount of visual improvement or reduction in macular edema would be explained by more studies with longer follow-up.

#### **V. Conclusion**

Intravitreal Dexamethasone implant appears effective in management of persistent macular edema due to retinal vascular disease with high safety level, but improvement persists for a transient period – maximum up to 4 months. Early detection and treatment may provide a better outcome.

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Legend to figures:

Fig – 1: Retinal vascular diseases pattern

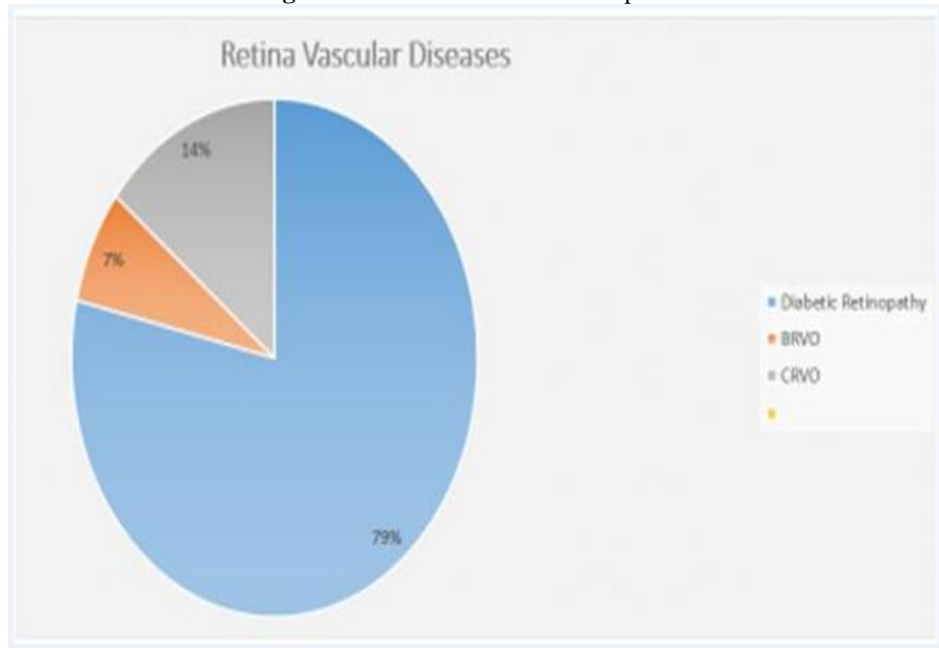


Fig – 2: Mean central macular thickness at 0, 1 and 4 months

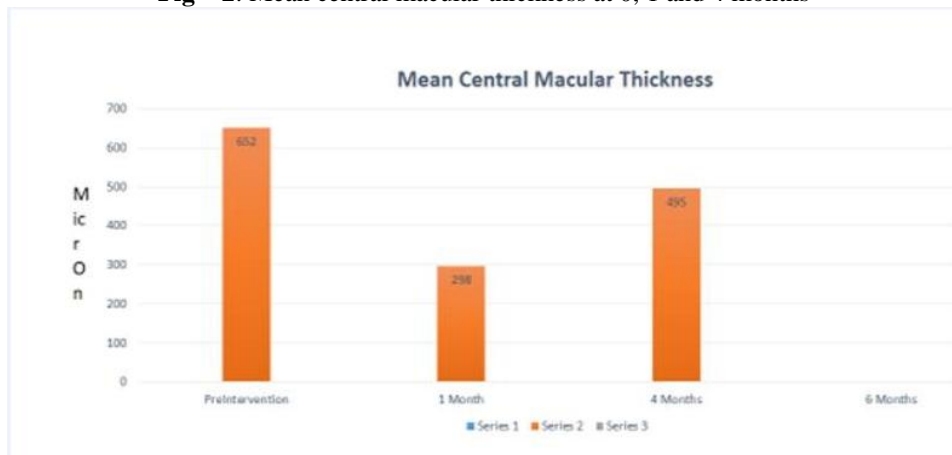
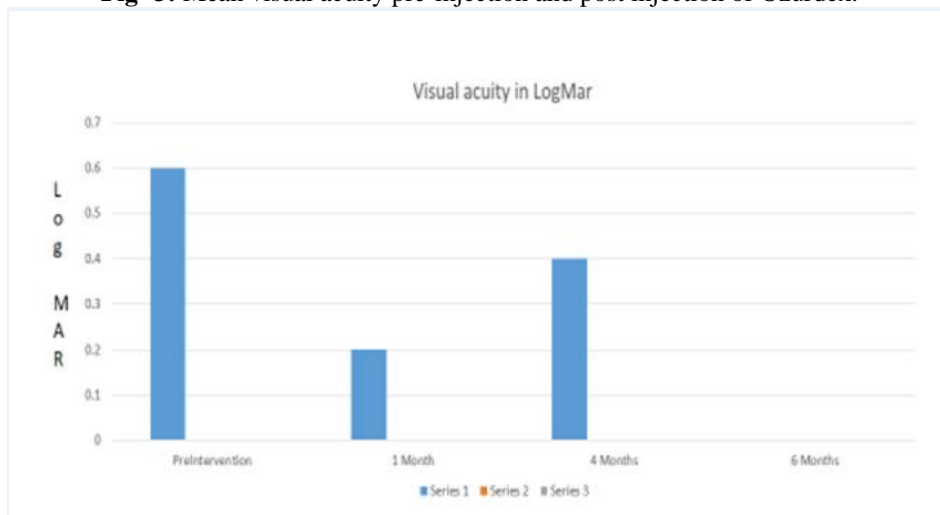


Fig- 3: Mean visual acuity pre-injection and post injection of Ozurdex.



**Legend to tables:**

Treatment options	Numbers ( Percentage )
Multiple AntiVEGF	2
Laser	0
AntiVEGF + Laser	12

**Table - 1:** Pre Ozurdex intervention history

\*Arunava kundu. "Outcomes of Intravitreal Dexamethasone Implant in Persistent Macular Edema Due to Retinal Vascular Diseases Intravitreal Dexamethasone Implant in Persistent Macular Edema." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.10 (2017): 78-82