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A RETROSPECTIVE OBSERVATIONAL STUDY OF INTRAVITREAL OZURDEX IMPLANT IN TREATING MACULAR PERSISTEN EDEMA

CRISTIAN TURLEA[1],MAGDALENA TURLEA[1],ILEANA ZOLOG[4], PAVEL FARCAS[2], ANDREI BRANCO TOMESCU[3]

[1]Department of Ophthalmology ,West University"Vasile Goldis" Arad
[2]The Faculty of Economics, West University"Vasile Goldis" Arad
[3]Department of General Surgery, West University"Vasile Goldis" Arad
[4]Department of Ophthalmology ,University of Medicine and Pharmacy"Victor Babes" Timsioara

ABSTRACT. This retrospective study evaluates the efficacy of intravitreal implant with dexamethasone (Ozurdex®; Allergan Inc, Irvine, CA, USA) in the treatment of patients with persistent macular edema of different etiology. We evaluated 13 eyes of 13 patients who where diagnosed with macular edema of different aetiology and treated with a single intravitreal implant of Ozurdex with a follow-up of six months. The effects of the intravitreal implant where evaluated by best correction visual acuity(BCVA), central macular thickness(CMT) during a follow-up of 6 months. The mean baseline BCVA and standard deviation(STD) was 0,25±0,19 and after 6 months it was 0,60±0,24. The mean baseline CMT evaluated by optical coeherence tomography(OCT) was 556±145µ and after 6 months it decreased to a value of 275±68µ. There where no serious side effects, but for a temporary raise of intraocular pressure(IOP) in 4 patients,who responded to topical antihipertensive eyedrops and 2 patients who developed cataract. Intravitreal implants with Ozurdex have proven significant improvement in BCVA and CMT in patients with macular edema in a period of six months without any serious sight threatening events.
KEY WORDS: Inravitreal implant,Macular edema,Ozurdex,dexamethasone

INTRODUCTION

Macular edema(ME) is a non – specific sign of several retinal vascular diseaseases that lead to central vision loss.

ME is the result of fluid accumulation in the retinal layers across the fovea. Among the most frequent causes of ME are diabetic retinophaty(DR) and retinal vein occlusions(RVO).

DR is the most common cause of vision loss in developed countries. It is estimated that in 2011 28,5 million americans suffer from diabetes and 25% of these will develop a form of DR and 4 % will develop diabetic macular edema(DMA) leading to central vision loss (Zhang X, Saaddine JB, Chou CF, et al. Prevalence of diabetic retinopathy in the United States, 2005–2008. JAMA. 2010;304:649–56). After DR ,retinal vein occlusion is the second most common vascular retinophaty that leads to vision loss by developing ME. The most common type is branch RVO followed by central RVO. Both ME caused by DR or RVO have a gold standard therapy represented by grid laser retinal photocoagulation (Rogers S, McIntosh RL, Cheung N, et al: The prevalence and number of people with retinal vein occlusion: pooled data from population-based studies from the US, Europe, Australia and Asia. Ophthalmology 2010;117:313–319.e1).

Laser therapy proved to be effective in preserving visual acuity ,but it is accompanied by visual field loss, contrast disturbance and color loss. In the last decade a series of other treatments have emerged that have improved the treatment for ME, and even have lead to a gain in visual acuity. These treatments are based on intravitreal injections containing anti vascular endothelial growth factor(VEGF) or corticosteroids. In the 2012 the first intravitreal anti VEGF factor Ranibizumab(Lucentis,Novartis inc.) was aproved by the F.D.A. to be used in ME in DR and RVO. Studies confirmed its effect in improving vision in patients with ME, being andiminstered as one injection for 3 months (Shamsi HNA, Masaud JS, Ghazi NG. Diabetic macular edema:New promising therapies. World J Diabetes 2013; 4(6): 324:338).

Corticosteroids where also introduces for the treatment of ME ,especialy in persisten chronic forms of the disease. They have an effective antinflammatory and anti VEGF action and contribuiting to the stability of the blood retinal barrier. The first corticosteroid usedd as a intravitral injection in ME was Triamcinolon, 4mg ,used off label. Studies showed similar efects as Ranibizumab (Sutter FK, Simpson JM, Gillies MC. Intravitreal triamcinolone for diabetic macular edema that persists after laser treatment: three-month efficacy and safety results of a prospective, randomized, double-masked, placebo-controlled clinical trial. Ophthalmology 2004; 111: 2044-2049).

Ozurdex(Allergan,inc.), containing 0,7 mg of dexamethasone is a sustained-release intravitreal biodegradablel implant that has been approved recently to be used in the treatment of ME in DR and RVO. Studies have confirmed it's efficacy and prolonged action for up to 6 months with little side-effects. Intravitreal use of Ozurdex has been approved in 2012 for the treatment of RVO with ME and recently for patients with diabetic macular edema(DME) and posterior uveitis. This new intravitreal implant could more cost effective then intravitreal injections with anti VEGF molecules,who for a sustained effect have to be administered for 3 months (Kuppermann BD, Chou C, Weinberg DV, Whitcup SM, Haller JA, Blumenkranz MS; Dexamethasone DDS Phase II Study Group. Intravitreous dexamethasone effects on different patterns of diabetic macular edema. Arch Ophthalmol. 2010;128(5): 642–643).

MATERIAL AND METHODS

The aim of this retrospective observational study is to evaluate the efficacy of intravitreal implant containing 0,7 mg Ozurdex in the treatment of DME and ME caused by RVO.

The study was comprised of 13 patients with an average age of 60 , 9 patients being male and 4 female.The inclusion criterias where patients over 18 years of age, clinical persistent macular edema diagnosed by OCT examination with a CMT≥250µ , a best correction visual acuity(BCVA) between 0,01 and 0,6. Patients with other ocular patologies like cataract,uveitis, glaucoma or other ocular infections where excluded from the study.

All patients had previous laser photocoagluation treatment in the last 6 months with no significant results.

All intravitreal implants where carried out in sterile conditions in the operating theater. Injections where administered at 4 mm from the limbus and at 3,5 mm if the patients eye is pseudophakic.

After the implant is administered patients are given antibiotics eye drops for a week. Controls where caried out at baseline, 3 months and 6 months.

RESULTS

A total of 13 patients have been enrolled in this retrospective short –time study to evaluate the efficacy of a dexamethasone(Ozurdex) 0,7 mg in patients with macular edema with different etiology.The mean age of the patients was 60±7.14, 4 patients where female and 9 where male. From the aetiology point of view, 4(30,77%) patients had DME and the other 9(69,23%) had RVO.From the patients wih RVO, 3 had central retinal vein occlusion(CRVO) and the other six where diagnosed with branch retina vein occlusion(BRVO).

At base line all patients had OCT scand performed and BCVA recorded. The mean basline BCVA was 0,25±0,19 (range 0,01-0,6) and mean CMT was 556±145µ (range 410-931). Each patient was administered one intravitreal implant with Ozurdex, BCVA was recorded at baseline, 3 and 6 months and CMT wa recorded at baseline and at 6 months.

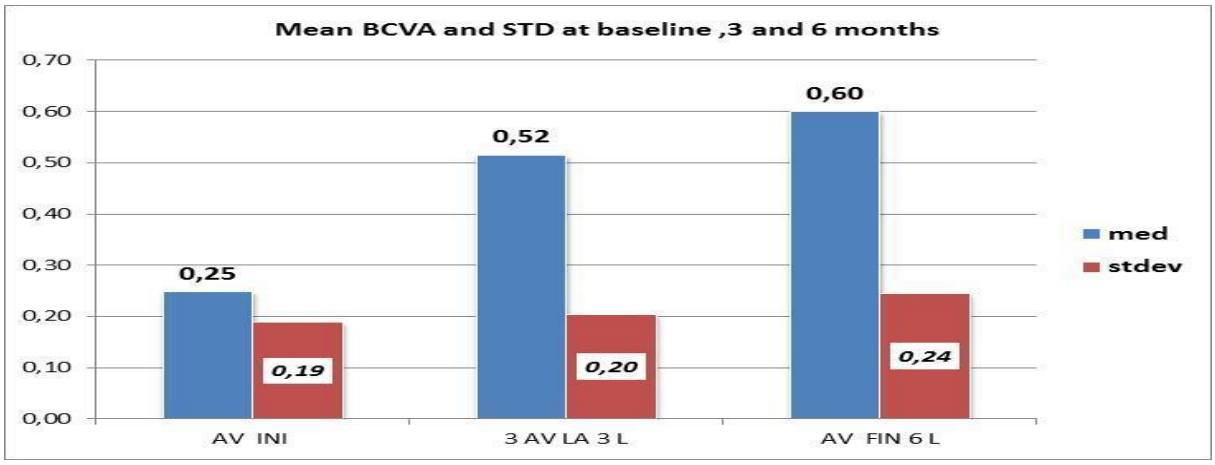

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Fig.1 Mean BCVA and STD at baseline,3 and 6 months after intravitreal Ozurdex implant

The mean BCVA at 3 months was 0,52±0,20 and at 6 months it was 0,60±0,24.All patients have gained more than 2 lines and a mean of 0,35±0,17 in BCVA(Fig.1) on the Snellen chart and none lost any letter in terms of visual acuity.

After 6 months there was a mean loss of macular tickness measured by OCT of 280±126,35μ and a mean CMT of 275±65μ.(Fig.2)

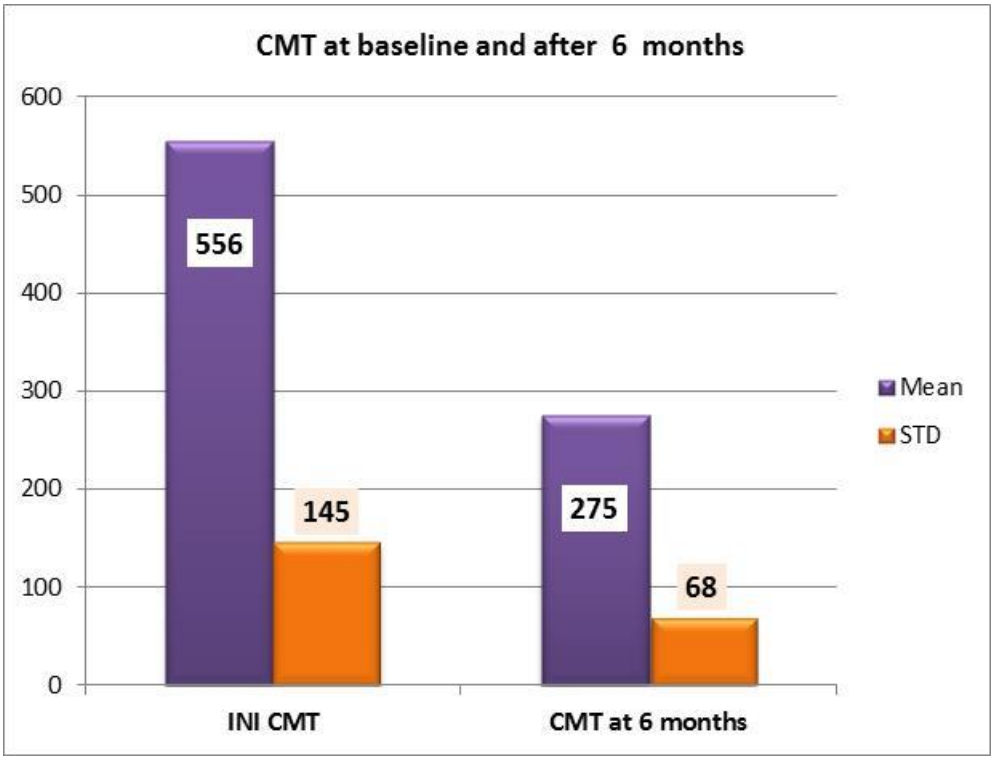
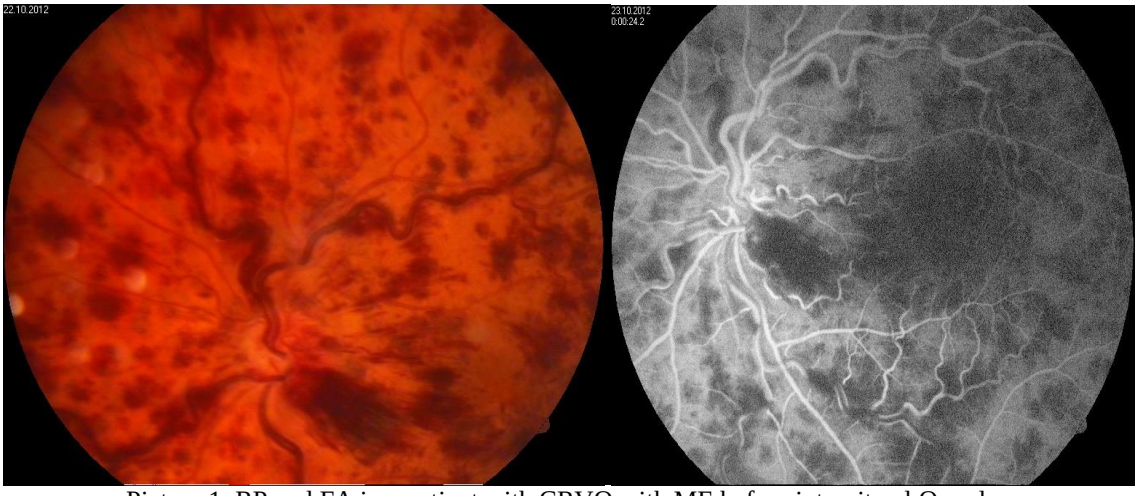
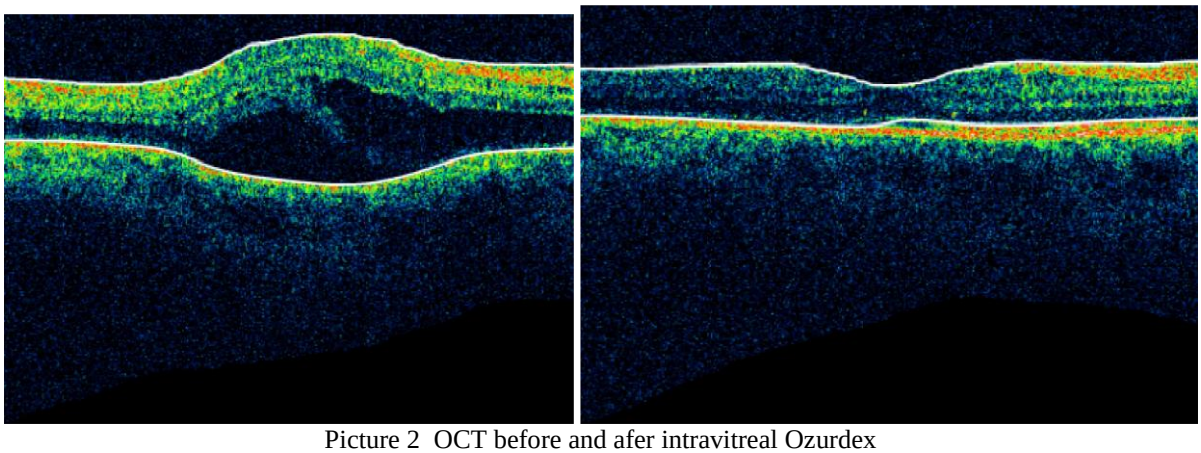


Fig.2 CMT at baseline and after 6 months

All patients had retinal photography(RP) and flourescein angiography(FA) and OCT(Pic.2) done at baseline and after 6 months.All these investigations demonstrate the positive role of Ozurdex in the treatment of ME.(Pic.1)



Picture 1 RP and FA in a patient with CRVO with ME before intravitreal Ozurdex



Picture 2 OCT before and afer intravitreal Ozurdex

After the intravitreal treatment with Ozurdex from 13 patients , 5 patients have experienced high IOP above 24 mmHg, and where treated with topical eyedrops. After 6 months 2 patients developed cataract and where programed for surgery later on. No patient had lower VA at 6 months than he had in baseline.

DISCUSSIONS

This short retrospective observasional study confirms that slow release implant with intravitreal Ozurdex in patients with persistent ME with DR and RVO is effective even after 6 months in terms of VA and the reduction of CMT. Other studies alo confirm the gain in BCVA of at least 3 lines on the Snellen chart. The mean reduction of CMT aslo is found in other authors with short term obersvational studies(Haller JA, Bandello F, Belfort R Jr, et al; OZURDEX GENEVA Study Group. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology 2010;117:1134–46).

Most other studies evaluate only patients with diabetic macular edema or ME after RVO separately, while in our study patients have both etiologies leading to a low VA.

Other stduies confirm that the effect of Ozurdex is seen at 4 weeks after implantation and lasts about 16 weeks , our study confirms that it even lasts 24 weeks. The low number of patients and the short follow up time of only 6 months can not fully evaluate in time the effects of the intravitreal treatment as have other long-term studies confirmed. The literature has shown that usually after 6 months the action of Ozurdex declines, its vitreous concentrations decreases (Zucchiatti I, Lattanzio R, Queques G, et al. Intravitreal dexamethasone implant in patients with persistent diabetic macular edema. Ophthalmologica. 2012;228:117–122).

The recently published Bevordex study comparing Ozurdex with Avastin(Bevacizumab) in a period of 12 months proved that one implant of dexamethasone is equal to 3 intravitreal Bevacizumab injections. Similar results where obtained in terms of BCVA ,but in regarding CMT Ozurdex proved to be more efficient. In the Ozurdex group more patients lost VA because of developing cataract ,as was in our study. The low number of patients in our study is related to the expensive cost of Ozurdex implant and is a limitation of our study.

Besides the treatment , the follow-up by OCT examinations where also expensive and not all patients agreed to have it done (Mark C. Gillies, MBBS, PhD, Lyndell L. Lim, MBBS, Anna Campain, PhD,1 Godfrey J. Quin, MBChB, PhD,Wedad Salem, MB BS, MPH, Ji Li, MB BS, Stephanie Goodwin, BAppSc (Orthoptics) (Hons),Christine Aroney, MBBS, Ian L. McAllister, MBBS, Samantha Fraser-Bell, MBBS, PhD, A Randomized Clinical Trial of Intravitreal Bevacizumab versus Intravitreal Dexamethasone for Diabetic Macular Edema The BEVORDEX Study. Ophthalmology 2014;121:2473-2481).

CONCLUSION

Ths intravitreal slow-release implant with Ozurdex is effective in reducing CMT and gaining and maintaining BCVA in patients with ME caused by DR and RVO. Our study confirms that for at least 6 months these functional and anatomical changes are valid with no serious side effects.

Intravitreal steroids are efficient especially then when laser can not improve VA in patients with ME. Dexamethasone implant has the same impact as 3 anti VEGF injections in terms of improving VA. All these treatments have certain limitations and have to be repeated when ever it is needed.

In our country these treatments,are expensive and not covered by national health inssurance and so they can reach just few patients.

There is a need for a national health plan that can inccorporate these new treatments, so that all patients suffering from ME can benefit.

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Corresponding adress: dr.turlea@gmail.com