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Response of Postoperative and Chronic Uveitic Cystoid Macular Edema to a Dexamethasone-Based Intravitreal Implant (Ozurdex)

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Abstract

Purpose: To survey the clinical responses to treatment of chronic postoperative and uveitic cystoid macular edema (CME) with a dexamethasone-based intravitreal implant (Ozurdex®).
Methods: This retrospective, interventional case series reports on patients with chronic CME after uncomplicated vitrectomy for epiretinal gliosis or phacoemulsification (group 1: 12 eyes) or secondary to noninfectious endogenous uveitis (group 2: 36 eyes). Central retinal thickness (CRT), best-corrected visual acuity (BCVA, logMAR), and intraocular pressure (IOP) throughout follow-up were gleaned from the medical records.
Results: In group 1, CRT decreased, compared with baseline, from 519 ± 43 to 297 ± 23 and $356 \pm 49\,\mu m$ by the 1- and 3-month visit ($P = 0.02$) and to $429 \pm 57\,\mu m$ before reimplantation. In group 2, CRT decreased from 460 ± 31 to 300 ± 21 and $312 \pm 26\,\mu m$ by the 1- and 3-month follow-up, respectively ($P = 0.001$), and to $373 \pm 32\,\mu m$ before reimplantation. Complete resolution of CME was achieved in 67% and 94% (groups 1 and 2, respectively) by 1 month and in 42% and 80% by 3 months after injection. In group 1, BCVA improved from 0.46 ± 0.08 to 0.27 ± 0.09 and 0.20 ± 0.06 ($P = 0.01$) by the 1- and 3-month follow-up, respectively, and to 0.32 ± 0.08 before reimplantation. In group 2, BCVA improved from 0.47 ± 0.06 to 0.34 ± 0.09, 0.26 ± 0.07, and 0.29 ± 0.08 ($P < 0.05$) at 1 and 3 months of follow-up and before reimplantation, respectively. A significant IOP increase was not observed in either group. Mean time to reimplantation of Ozurdex was 6.4 ± 5.7 and 6.6 ± 3.4 months for postoperative and uveitic CME, respectively.
Conclusion: Ozurdex seems to achieve a sustained effect over up to 6 months in postsurgical and uveitic CME.

Introduction

Macular edema can result from a variety of inflammatory and noninflammatory retinal disorders, such as uveitis, or occur after an intraocular surgical intervention, such as vitrectomy or cataract surgery.

The appearance of cystic macular edema after an intraocular intervention is usually successfully treated with topical anti-inflammatory agents and often self-limiting after 6–12 months. Eyes with persistent cystoid macular edema (CME) despite prior therapy are at risk for permanent visual loss. The underlying pathogenesis still remains undetermined.[1]

The prevalence of clinically significant pseudophakic cystoid macular edema (PCME) has declined in the past decade due to the introduction of minimally invasive small incision cataract surgery and phacoemulsification. Despite this fact, PCME still remains a challenge as cataract surgery is being performed at a very high number all over the world so that the incidence of this postoperative morbidity remains relevant. Chu et al. report an incidence of 1.2% after uncomplicated phacoemulsification surgery. After capsular rupture with or without vitreous loss, the risk of PCME development is increased, and in the presence of diabetic retinopathy it may be increased by fourfold.[2]

Since epiretinal membrane (ERM) formation is primarily associated with diffuse or CME, the surgical trauma of pars plana vitrectomy for ERM removal usually goes along with CME. Persisting CME despite topical therapy seems to be increased with preoperative intraretinal cysts, and newly developed postoperative CME has to be expected in about 10%.[3]

Uveitis may be associated with a variety of infectious and immunoregulatory diseases, however, the underlying etiology

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is often unknown. In chronic uveitis, macular edema is the most common cause for visual impairment, making it—even after control of the inflammatory activity—a sight-threatening disease, which compromises the quality of life of the affected individuals, who are often of working age.[4]

A therapeutic handling of macular edema aims to reduce the inflammatory response and to prevent the damage to the ocular structures that would result in a long-term loss of vision. A topical application or a local injection of corticosteroids is the preferred strategy for unilateral intermediate and posterior-segment noninfectious uveitis. In severe cases, systemic treatment with either corticosteroids or other immunomodulatory agents is called for; however, systemic immunosuppressive therapy is associated with a broad range of generalized side effects.

Although repeated intravitreal injections of corticosteroids, such as triamcinolone, are used with the intention to control inflammation in eyes with uveitic or postoperative CME, their instrumentation is associated with a rapid progression of cataracts and a secondary rise in intraocular pressure (IOP).[5,6] With a view to reduce the injection burden and side effects, sustained-release intraocular corticosteroid implants have been developed.[7] One such implant is Ozurdex® (Allergan, Inc., Irvine, CA), which delivers a 0.7 mg-dose of dexamethasone to the vitreous cavity, and has been shown to improve the clinical outcome by ameliorating vision and reducing the central retinal thickness (CRT).[8] A large prospective randomized clinical trial has been undertaken to demonstrate the efficacy and the safety of Ozurdex (Huron trial).[9] In this study, the effects of the implant, with its 0.7 mg burden of dexamethasone, were compared with those elicited by a 0.35 mg injection of the drug and to sham in eyes with chronic uveitic CME ($n=229$) over a follow-up period of 26 weeks. Ozurdex was well tolerated and elicited a notable suppression of intraocular inflammation over a time of 6 months.

Since only a few long-term trials have been undertaken to evaluate the efficacy and the safety of multiple injections of dexamethasone,[10] especially regarding postoperative CME, we retrospectively evaluated the mid-term effect of Ozurdex on the anatomical and the functional outcomes in genuine cases of postoperative and uveitic macular edema that evinced no obvious signs of inflammation.

Methods

The study protocol for this retrospective multicenter cohort study, involving 48 eyes (40 patients), was approved by the Institutional Review Boards of the respective Clinical Ethics Committees and was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients and power analysis was performed.

Patients had to be monitored for a minimal follow-up period of 6 months. Anatomical response (change in CRT) was defined as the primary study outcome parameter, whereas the time until reimplantation, the change in visual acuity, and the side effects were taken as the secondary ones. Measurements of CRT (determined in μm by OCT, Spectralis™; Heidelberg Engineering, Heidelberg, Germany), best-corrected visual acuity ([BCVA] determined on a logarithmic scale and converted to logMAR values), and IOP (mmHg, measured by Goldmann applanation tonometry) were performed before Ozurdex placement, 1 and 3 months thereafter, and before reimplantation. Data appertaining to the anatomical and the functional outcomes were extracted from patients' medical records. We evaluated the treatment as good anatomical outcome if there was a reduction of retinal thickness by more than 20% and/or a complete resolution of macular edema was achieved.

All patients included in this series were suffering from postoperative (group 1) or inflammatory (group 2) CME associated with a noninfectious chronic endogenous uveitis and had been pretreated for a minimum of 3–6 months with local and, in some instances, also systemic steroids and/or immunomodulating agents to control their inflammatory disease and a secondary CME. In all cases, the secondary CME was irresponsive to this therapy before considering intravitreal steroids.

Therapy-refractive CME was the only postoperative problem that was encountered in eyes that had undergone vitrectomy for ERMs ($n=9$). All of these eyes had been primarily pseudophakic or had undergone combined cataract surgery and vitrectomy. Eyes that had developed CME after uncomplicated cataract surgery ($n=3$) had evinced no signs of a pre-existing macular pathology, such as vitreomacular traction or epiretinal gliosis (group 1). In group 2 cases, uveitis was well controlled, the affected eyes showed a vitreous haze score of or below 1 according to the Standardization of Uveitis Nomenclature (SUN) criteria at all time points.[11]

In addition to the measurements of CRT, BCVA, and IOP, data appertaining to the treatment indications, the diagnosis of uveitis, the status of the lens, the number of injections, the time to reinjection, systemic treatment strategies, and complications were collected.

The numerical data are presented as mean values together with the standard deviation (SD) or standard error of the mean (SEM) and were statistically evaluated using Student's *t*-test. Differences between groups were considered to have attained statistical significance (*) or high significance (**) if the *P*-value lay below 0.05 or 0.01, respectively. Probabilities of events occurring after the first intravitreal dexamethasone implant injection are diagramed as survival curves using the Kaplan–Meier method. Construction of the Kaplan–Meier survival analysis curves was performed using MedCalc 15.11.4 software (MedCalc software, Ostend, Belgium).

Results

In this retrospective multicenter cohort study, involving 48 eyes (40 patients), Ozurdex-treated patients were followed over a period of 13 ± 9 months in cases either of postoperative macular edema that had not responded to standard treatment regimens (group 1, $n=12$ eyes) or noninfectious uveitis (group 2, $n=36$ eyes).

At the time of the first intravitreal Ozurdex implant, 40 of the 48 eyes in the study cohort were pseudophakic.

Nine out of 12 (75%) in group 1 and 10 out of 36 eyes (28%) in group 2 had undergone vitrectomy before the first placement of Ozurdex. In group 1 and group 2 patients, this intervention had been performed 32 ± 30 and 22 ± 14 months, respectively, before the first Ozurdex placement.

The mean age of the patients in groups 1 and 2 were 72 ± 7 and 53 ± 18 years, respectively ($P=0.0009$). The mean duration of CME before Ozurdex implantation after either uncomplicated vitrectomy for epiretinal gliosis or cataract surgery (group 1) was 25 ± 22 months, and for that secondary to uveitis 38 ± 31 months (group 2). Before the

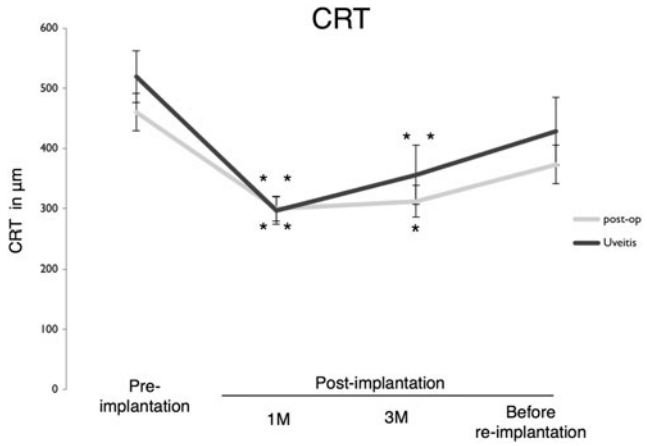

FIG. 1. CRT in µm: before the first implantation of Ozurdex®, 1 and 3 months later and before a reimplantation. *Light gray*: cases of postoperative CME ($n = 12$ eyes in 12 patients); *dark gray*: cases of uveitic CME, irrespective of whether vitrectomy had or had not been performed ($n = 36$ eyes in 28 patients). *$P \leq 0.05$; **$P \leq 0.01$. Error bars represent SEM. CME, cystoid macular edema; CRT, central retinal thickness; SEM, standard error of the mean.

first Ozurdex implant, patients in group 1 had received 2.1 ± 3.8 intravitreal injections (in total 26 injections, 85% triamcinolone, and 15% anti-VEGF), those in group 2, 1.8 ± 5.5 intravitreal injections (in total 63 injections, of which 87% were triamcinolone and 13% anti-VEGF). In total, in group 1 patients, 43 Ozurdex implants were performed in 12 eyes over a period of 21 ± 11 months. In group 2 patients, 47 Ozurdex implants were placed in 36 eyes over a period of 10 ± 5 months.

In group 1, CRT decreased from 519 ± 43 µm, before the first Ozurdex placement, to 297 ± 23 µm by the first month, by the third month, it newly increased to 356 ± 49 µm ($P = 0.02$), and further to 429 ± 57 µm before a reimplantation. In group 2, CRT decreased from 460 ± 31 µm, before the first Ozurdex placement, to 300 ± 21 µm by the first month and to 312 ± 26 µm by the third month ($P = 0.001$), before it again increased to 373 ± 32 µm before reimplantation (Fig. 1). Complete resolution of CME was achieved in group 1 in 67% of eyes and in group 2 in 94% by the 1-month visit and in 42% and 80% by the 3-month follow-up.

A single implant was placed in 2 out of 12 eyes (17%) in group 1 and in 12 out of 36 eyes (33%) in group 2, and multiple ones in 83% and in 67% of the eyes, respectively. The mean duration until reimplantation of Ozurdex was 6.4 ± 5.7 months and 6.6 ± 3.4 months in group 1 and group 2 eyes, respectively.

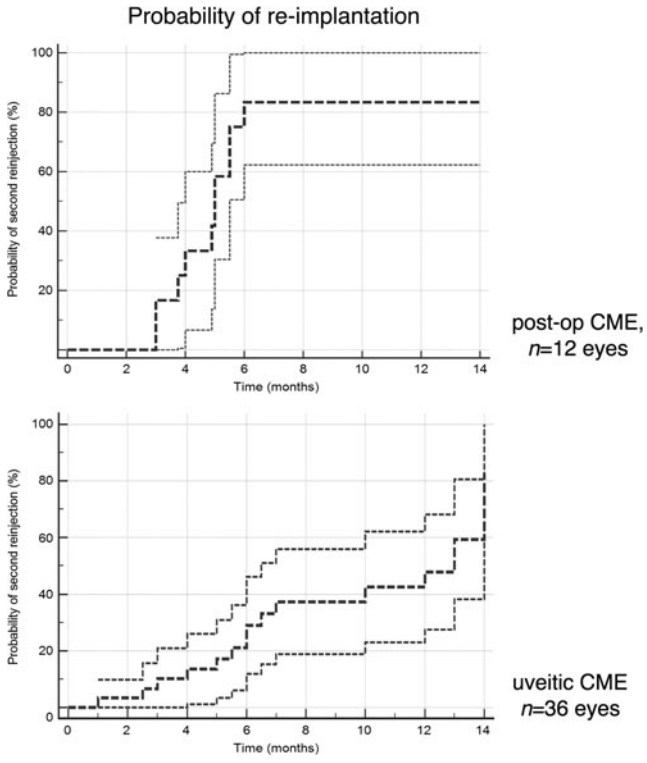

FIG. 2. Kaplan–Meier survival analysis of time to repeated intravitreal dexamethasone implant injections after first implant injection in postoperative and chronic noninfectious uveitis eyes. (postoperative $n = 12$ eyes, uveitis $n = 36$ eyes); *dotted fine lines* = 95% confidence intervals; formula = median time to second injection.

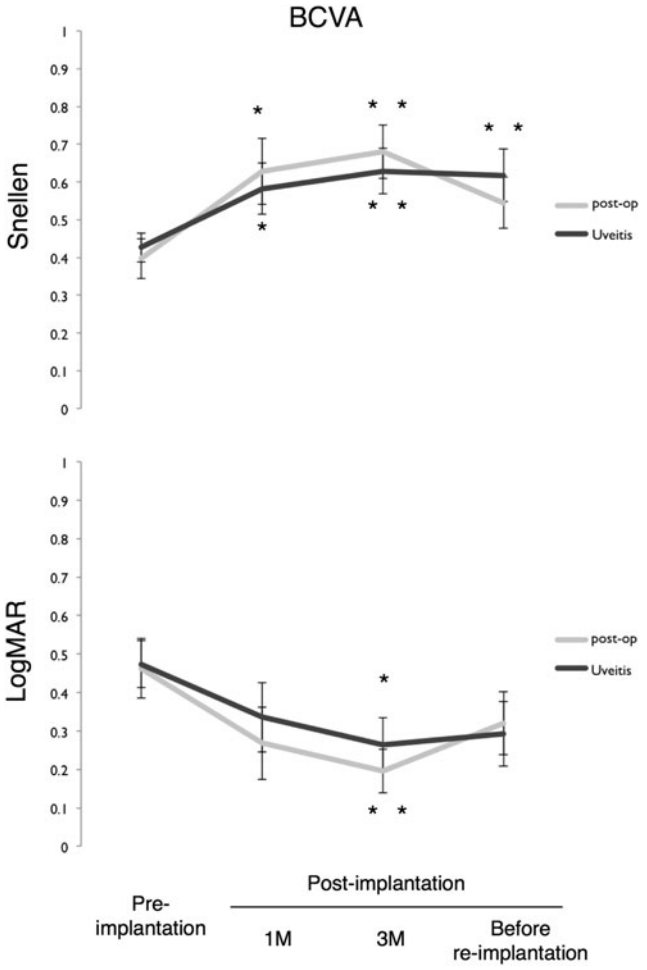

FIG. 3. BCVA on a Snellen scale (*upper row*) and in logMAR units (*lower row*): Before the first implantation of Ozurdex®, 1 and 3 months later and before a reimplantation. *Light gray*: cases of postoperative CME ($n = 12$ eyes, 12 patients); *dark gray*: cases of uveitic CME, irrespective of whether vitrectomy had or had not been performed ($n = 36$ eyes, 28 patients). *$P \leq 0.05$; **$P \leq 0.01$. Error bars represent SEM. BCVA, best-corrected visual acuity.

Table 1. Anatomical and Functional Information Appertaining to the Different Groups

	Group 1 Postoperative CME (n = 12), mean ± SEM	*Group 2a Uveitic CME (no vitrectomy) (n = 26), mean ± SEM*	*Group 2b Uveitic CME (vitrectomy) (n = 10), mean ± SEM*
CRT (μm)			
Preimplantation	519 ± 43	439 ± 32	513 ± 74
1 month	297 ± 23	306 ± 29	285 ± 13
3 months	356 ± 49	328 ± 42	286 ± 13
Before reimplantation	429 ± 57	369 ± 42	383 ± 46
BCVA (logMAR)			
Preimplantation	0.46 ± 0.08	0.44 ± 0.06	0.57 ± 0.15
1 month	0.27 ± 0.09	0.31 ± 0.09	0.39 ± 0.24
3 months	0.20 ± 0.06	0.25 ± 0.09	0.30 ± 0.11
Before reimplantation	0.32 ± 0.08	0.29 ± 0.12	0.30 ± 0.10
IOP (mmHg)			
Preimplantation	15 ± 1	13 ± 1	13 ± 1
1 month	16 ± 1	14 ± 1	15 ± 1
3 months	16 ± 1	14 ± 1	14 ± 2
Before reimplantation	15 ± 1	14 ± 2	13 ± 1

BCVA, best-corrected visual acuity; CME, cystoid macular edema; CRT, central retinal thickness; IOP, intraocular pressure; SEM, standard error of the mean.

The Kaplan–Meier analysis (Fig. 2) estimates the probability of a second dexamethasone implantation. Accordingly, 50% would require a second implant after 5 months and after 6 months in groups 1 and 2, respectively.

In group 1 mean logMAR BCVA improved from 0.46 ± 0.08, before the first Ozurdex placement, through 0.27 ± 0.09 to 0.20 ± 0.06 by the first and the third months, respectively ($P = 0.01$) and then decreased to 0.32 ± 0.08 before a reimplantation. In group 2, the mean BCVA (logMAR) ameliorated from 0.47 ± 0.06, before the first Ozurdex placement, through 0.34 ± 0.09 to 0.26 ± 0.07 ($P = 0.04$) by the first and the third months, respectively, and then fell back to 0.29 ± 0.08 before a reimplantation (Fig. 3). A 2 or more line improvement was seen in 27% at 1 month after implantation, in 30% at 3 months after implantation, and in 27% before reimplantation in group 1, whereas in group 2 a 2 or more line improvement was observed in 47% at the 1-month visit, 44% at the 3-month follow-up, and 41% before reimplantation. With respect to visual improvements, changes in CRT, rises in IOP, and duration of the Ozurdex-induced effect, no differences were observed between vitrectomized and nonvitrectomized eyes in group 2 (Tables 1 and 2).

No significant increase in IOP was observed in either of the groups or sub-groups (Fig. 4a, b). Rises of IOP were medically controlled by the administration of no more than 2 new antiglaucoma agents in 2 of the 12 eyes (13%) in group 1 and in 4 of the 36 group 2 eyes (11%). In one eye with uveitic CME and a retropupillary iris claw (Artisan®) intraocular lens, the implant spontaneously dislocated into the anterior chamber. However, after a pharmacologically induced dilation of the pupil, it could be relocated and did not newly dislocate. No other adverse events were recorded.

Discussion

Dexamethasone is implemented in the treatment of many ophthalmological diseases, such as retinal vein occlusion-associated macular edema, diabetic macular edema, noninfectious uveitis, Irvine-Gass syndrome, and age-related macular degeneration (adjunctively). However, its use is associated with several adverse consequences, first and foremost among which are rises in IOP and the formation of cataracts.[12] The safety profile of Ozurdex is better, and until now it has a longer lasting effect than the most frequently

Table 2. Three-Month Outcome After Ozurdex Implantation and Duration Effect

Groups	n *(eyes/ patients)*	*CRT-change (%) 3 months after Ozurdex implantation*	*BCVA-change 3 months after Ozurdex implantation*	*IOP-change 3 months after Ozurdex implantation*	*Duration of effect (months), mean ± SD*
Group 1: postoperative CME	12/12	32% Reduction	2.5-Line improvement	1 mmHg increase	6.4 ± 5.7
Group 2: all cases of uveitic CME (vitrectomized and nonvitrectomized)	36/28	32% Reduction	2-Line improvement	2 mmHg increase	6.6 ± 3.4
Group 2a: uveitic CME (no vitrectomy)	26/19	25% Reduction	2-Line improvement	1 mmHg increase	6.6 ± 3.3
Group 2b: uveitic CME (vitrectomy)	10/9	44% Reduction	2.5-Line improvement	1 mmHg increase	6.1 ± 3.0

SD, standard deviation.

Table 3. **(A, B)** Published Evidence of Treatment with Ozurdex in Uveitic Macular Edema

A

First author (year of publication)	n *(eyes)*	n *(patients)*	*Study design: R, P, PR, NR*	*Duration of follow-up period (months)*	*Duration of ME before therapy (months)*	*Characteristics of edema: chronic (c), persistent (p), undetermined (u)*	*Pretreatment: N, A, T, L, Others*
Lowder (2014)[9]	O 0.35 mg: 76 O 0.7 mg: 77 Sham: 76	229	P, PR multicenter	6.5	n.r.	u	n.r.
Tomkins-Netzer (2014)[10]	38	27	R	17	n.r.	u	18 (T), 4 (Methotrexate)
Zarranz-Ventura (2014)[17]	82	63	R multicenter	35	n.r.	u	46 (T), 16 (T)
Adán (2013)[25]	17 (vitrectomized)	13	R	9.6	12	p	5 (T),7 (T)
Arcinue (2012)[13]	Ozurdex 0.7 mg: 11 RETISERT: 16	25	R	>6	n.r.	u	n.r.
Williams (2009)[20]	O 0.35 mg: 13 O 0.7 mg: 12 Sham: 14	41	PR	12	>3	p	n.r.
Miserocchi (2012)[21]	14	12	R	9	n.r.	Recalcitrant uveitis	n.r.
Myung (2010)[22]	6	4	R	5.25	n.r.	u	n.r.
Own patients	Group 1: 36 Group 2: 12	Group 1: 28 Group 2: 12	R	≥6	12	c, p	Group 1: 51 (T), 22 (A) Group 2: 21 (T), 5 (A)

B

First author (year of publication)	n *(eyes)*	n *(patients)*	*BCVA baseline (logMAR)*	*BCVA 90 days (logMAR)*	*CRT (μm) baseline*	*CRT (μm) 90 days*	*IOP max (mmHg), n=eyes*	n *(no. of eyes retreated); no. of inj.; retreatment interval (months)*
Lowder (2014)[9]	O 0.35 mg: 76 O 0.7 mg: 77 Sham: 76	229	O 0.35 mg: 0.85 O 0.7 mg: 0.85 Sham: 0.86	n.r.	O 0.35 mg: 339 O 0.7 mg: 344 Sham: 324	n.r.	IOP >35 mmHg in less than 5%	No retreatment
Tomkins-Netzer (2014)[10]	38	27	0.47 ± 0.05	n.r.	453.29 (33.57)	n.r.	>21 mmHg, $n=7$	38 Eyes, 61 dexamethasone implants. 6 months (range, 2–42 months)
Zarranz-Ventura (2014)[17]	82	63	0.68 ± 0.4	0.49 ± 0.5	469 ± 193	318 ± 149	IOP ≥21 mmHg (33/82)	82; 142; 6.6
Adán (2013)[25]	17 (vitrectomized)	13	n.r.	n.r.	462	350	In 47% increased IOP	8; —; 6.5

(*continued*)

Table 3. (Continued)

B

First author (year of publication)	n *(eyes)*	n *(patients)*	*BCVA baseline (logMAR)*	*BCVA 90 days (logMAR)*	*CRT (μm) baseline*	*CRT (μm) 90 days*	*IOP max (mmHg), n = eyes*	n *(no. of eyes retreated); no. of inj.; retreatment interval (months)*
Arcinue (2012)[13]	Ozurdex 0.7 mg: 11 RETISERT: 16	25	n.r.	n.r.	Ozurdex: 380 ± 124 RETISERT: 340 ± 141	n.r.	44% in the RETISERT group needed antiglaucoma treatment, none in the Ozurdex group	Ozurdex: 13 months RETISERT: 28 months
Williams (2009)[20]	O 0.35 mg: 13 O 0.7 mg: 12 Sham: 14	41	O 0.35 mg: 0.9 O 0.7 mg: 0.92 Sham: 0.78	n.r.	2 line improvement: O 0.35 mg: 5/12 O 0.7 mg: 7/13 Sham: 2/14	n.r.	Increase in IOP of 10 mm Hg or more: O 0.35 mg: 1 of 12 O 0.7 mg: 5 of 13 Sham: 0	No retreatment
Miserocchi (2012)[21]	14	12	0.60	n.r.	496	n.r.	Three eyes controlled with antiglaucoma treatment	No retreatment
Myung (2010)[22]	6	4	0.80	n.r.	n.r.	n.r.	Unchanged	2; —; 3.5
Own patients	Group 1: 36 Group 2: 12	Group 1: 28 Group 2: 12	Group 1: 0.47 ± 0.06 Group 2: 0.46 ± 0.08	Group 1: 0.29 ± 0.08 Group 2: 0.20 ± 0.06	Group 1: 460 ± 31 Group 2: 519 ± 43	Group 1: 312 ± 26 Group 2: 356 ± 49	Unchanged	Group 1: 36; 47; 6.6 Group 2: 12; 43; 6.4

A, anti-VEGF agents (intravitreal injections); inj., injection; L, Laser treatment; ME, macular edema; N, no pretreatment; n.r., not reported; NR, nonrandomized; O, Ozurdex; P, prospective; PR, randomized; R, retrospective; T, Triamcinolone (intravitreal injections).

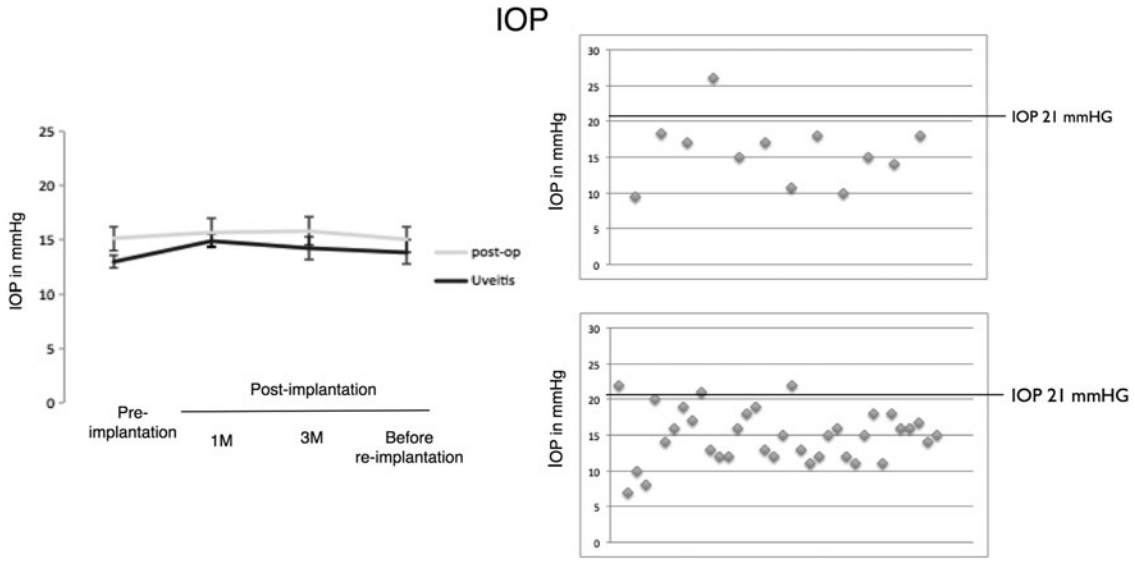

FIG. 4. **(a)** IOP in mm of mercury (mmHg): Before the first implantation of Ozurdex, 1 and 3 months later and before a reimplantation. *Light gray*: cases of postoperative CME ($n = 12$ eyes, 12 patients); *dark gray*: all cases of uveitic CME, irrespective of whether vitrectomy had or had not been performed ($n = 36$ eyes, 28 patients). $*P \leq 0.05$; $**P \leq 0.01$. Error bars are SEM. **(b)** IOP in mm of mercury (mmHg) 1 month after the first implantation of Ozurdex. *Upper row*: cases of postoperative CME ($n = 12$ eyes, 12 patients); *lower row*: all cases of uveitic CME, irrespective of whether vitrectomy had or had not been performed ($n = 36$ eyes, 28 patients). $*P \leq 0.05$; $**P \leq 0.01$. Error bars represent SEM. IOP, intraocular pressure.

used corticosteroid triamcinolone acetonide (TA).[13] Another corticosteroid that has been used for intravitreal applications is Fluocinolone acetonide (FA), which, in contrast to TA, exerts neuroprotective effects on the retina and the retinal pigment epithelium.[14,15] The MUST trial has demonstrated FA implants to be slightly more effective than systemic therapy when they are placed bilaterally. However, in cases of unilateral macular edema, local treatment strategies may be preferable.[5] The FA-containing RETISERT ® implant permits a release of the corticosteroid at a constant rate of 2.5 years. However, it needs to be surgically placed. Moreover, its use is associated with a very high risk of cataract formation and need for IOP-lowering surgery. Although the duration of the dexamethasone-induced effects is shorter than that of the RETISERT implant-induced ones, the agent seems to be better tolerated and its use is associated with fewer side effects and does not require surgical implantation.[13,16] Compared with these data, the beneficial safety outcome with an incidence of 11%–13% of IOP rise in our series seems favorable.

Moreover, our findings are concordant with those of Zarranz-Ventura et al.[17] who demonstrated that in 40.7% of their cases of noninfectious uveitis, a second placement of dexamethasone was necessary after a mean duration of 6.6 ± 1.9 months (Table 3), which is a longer time span than was called for in the handling of other ocular diseases. A third one was needed in 11.7% after 11 ± 1.5 months. An interesting finding of our own study adding to these data is that the mean duration until Ozurdex reimplantation was 6 months, not only in cases of uveitic CME, including those after vitrectomy, but also in those of postoperative CME.

To date, few publications refer to Ozurdex treatment in postoperative CME. Bellocq et al. and Mayer et al. report a recurrence of macular edema starting about 3 months after implantation. Regarding CRT, BCVA, IOP, and safety, both articles are well in line with ours[18,19] and demonstrate that repeated dexamethasone implantations show good effectiveness and no additional adverse events.

A prospective study from Williams et al. revealed a good safety profile for Ozurdex treatment with 0.35 or 0.7 mg dose for uveitic or postoperative CME with satisfactory visual improvements.[20] Smaller retrospective studies, likewise, showed an anatomic and functional improvement in persistent uveitic CME.[21,22]

In a retrospective case series conducted by Sorkin et al., including 37 eyes with persistent CME, eyes with uveitis ($n = 7$) demonstrated a faster CME resolution (2 weeks) and a longer CME-free period (20 weeks) than in retinal vein occlusion and diabetic macular edema as well as a similar efficacy for repeated Ozurdex injections.[23] Adding to these data, Tomkins-Netzer et al. reported that the accumulated effects of repeated implantations of dexamethasone result in continuous improvements in BCVA and CRT, with an ultimate stabilization of the latter.[10] Repeated implantations were performed in 63% of cases and led to a progression of posterior subcapsular cataract in 2 instances. In 7 of the eyes, a rise in IOP of more than 21 mmHg was recorded, but all responded well to pharmacological treatment.[10]

In another observational study, a consecutive series of 27 eyes in which CME persisted in the face of quiescent noninfectious intermediate or posterior uveitis was evaluated. In these cases, the BCVA (logMAR) improved from 0.60, before the dexamethasone implantation, to 0.41 at the 3-month juncture ($P = 0.0005$). The CRT decreased from 480 μm, before the dexamethasone implantation, to 280 μm at the 1-month juncture ($P < 0.0001$). These findings indicate that a dexamethasone implant is as effective in the suppression of inflammation in uveitis as in the treatment of uveitis-associated CME. Moreover, once again, no major complications were reported.[24]

In a retrospective case series of 17 eyes in 13 patients, who were suffering from persistent uveitic CME that had

been endured for 12 months, and who had a history of pars plana vitrectomy, the effects of dexamethasone implants were monitored for 9.6 months. CRT decreased from a preimplantation value of 462 μm through 277 μm at 4 weeks ($P < 0.01$) and 350 μm at 3 months ($P = 0.01$) to 394 μm at 6 months ($P = 0.14$). An improvement in the BCVA of ≥2 lines was recorded in 59% of eyes ($P < 0.01$). In 29% of the eyes, the anatomic and the functional gains were still apparent at 6 months. Similar to our results, repeated implantations were necessary in 47% of the eyes after a mean duration of 6.5 months.[25]

The findings of these studies compare favorably with our own and bolster evidence that the duration of the dexamethasone-induced effects persist longer in cases of uveitis, independent of vitrectomy, than do those that are elicited by other treatment modalities approved in Switzerland. Nevertheless, the risk for complications may be increased after vitrectomy. In vitrectomized patients, Adán et al. reported a higher-than-expected rate of side effects: ocular hypertension (47.1%), hypotony (11.8%), an anterior chamber displacement of the implant (5.9%), and glaucoma requiring filtration surgery (5.9%).[25]

In contrast to other ocular diagnoses most of the postoperative and uveitic cases of CME responded to 2 intravitreal implantations of dexamethasone, which were separated by a mean of 6 month interval, with satisfying anatomical and functional outcomes. Hence, implants of dexamethasone would appear to be an attractive treatment option for persistent postoperative and uveitic macular edema. The outcomes might have been better, if the therapy had been instigated before the structural damage had attained a level that rendered further improvements impossible. However, even in pretreated eyes with long-standing macular edema, which developed after vitrectomy for uveitis and after the removal of ERMs, a reduction of 32% in CRT and a 2-line improvement in the BCVA can be achieved.

The similar effects of Ozurdex in postoperative and uveitic cases of CME in our series are well compatible with experimental data suggesting that CME is mediated by inflammatory cytokines.[26,27]

In conclusion, we found, in accordance with published evidence, a satisfying anatomical response to treatment with significantly reduced macular edema in postoperative and uveitic CME over more than 1 year after repeated Ozurdex implantation. A functional gain, that is, a 2-line improvement in BCVA was observed remarkably beyond 3 months after implantation. Despite a decline of visual acuity thereafter, the majority of patients reported an improvement in the visual performance even after long-standing macular edema.

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Author Disclosure Statement

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