Outcome of Treating Pediatric Uveitis With Dexamethasone Implants

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• PURPOSE: To describe the outcome in children of eyes with uveitis following repeated treatment with dexamethasone (Ozurdex) implants.
• DESIGN: Retrospective, interventional study.
• METHODS: Twenty-two eyes of 16 pediatric patients with uveitis were treated with 35 dexamethasone implants at a tertiary referral center. Following implantations, anatomic and functional outcomes, as well as ocular complications, were noted. Main outcome measures included best-corrected visual acuity, central retinal thickness, number and dosage of systemic immunosuppression drugs, vitreous haze score, and presence of raised intraocular pressure or cataract.
• RESULTS: Following the first implantation, average best-corrected visual acuity improved significantly from 0.55 ± 0.08 logMAR to 0.37 ± 0.08 logMAR ($P = .024$), central retinal thickness decreased by 219 ± 55 μm ($P = .01$), and the percentage of eyes achieving a vitreous haze score of 0 increased from 41% to 88% ($P = .006$). The median time to relapse following the first injection was 9 months, with a similar response achieved after each repeat implantation. Children previously requiring systemic immunosuppression at the time of the first implantation were able to stop or significantly reduce the dose and number of drugs. In total there were 4 instances of cataract progression that were not visually significant and did not require surgical treatment and 6 cases of raised IOP, 5 of which were treated pharmacologically with no surgical intervention required and 1 that required revision of a previous filtration surgery. There were no cases of implant migration into the anterior chamber, endophthalmitis, or retinal detachment.
• CONCLUSIONS: The use of dexamethasone implants in children results in improved retinal thickness and reduction in ocular inflammation, which can improve vision for several months. Repeat implantations result in continued control of the inflammation, allowing for reduction of systemic immunosuppression with few ocular complications. (Am J Ophthalmol 2016;161:110–115. © 2016 by Elsevier Inc. All rights reserved.)

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UVEITIS ACCOUNTS FOR 10%–15% OF THE CAUSES OF blindness in the developed world. Though pediatric uveitis is relatively uncommon, accounting for only 5%–10% of all uveitis cases, vision-threatening complications are common, with a high rate of vision loss.[1–3] Ocular inflammation is treated aggressively in order to prevent the occurrence of ocular changes, such as cystoid macular edema (CME), vitreous inflammation, cataract, and retinal scarring, that may lead to vision loss.[4] Treatment is generally based on the use of systemic or regional corticosteroids, which are highly effective in controlling the inflammation, with the addition of second-line immunosuppression drugs in order to supplement the corticosteroids or as corticosteroid-sparing agents.[5] In children the treatment of uveitis is challenging mainly owing to the systemic side effects of these drugs, specifically corticosteroids, which can result in growth retardation, Cushingoid effects, behavioral changes, and related psychosocial problems.[6] Use of regional injections of periorbital corticosteroids and intravitreal triamcinolone acetonide reduces the need for systemic treatment and the risks of systemic side effects, while maximizing the ocular impact.[7–9] They are widely used in adults and to a lesser extent in children, mainly owing to their short effect and the need for repeat treatment under general anesthesia.[10,11]

Intravitreal dexamethasone implants (Ozurdex; Allergan, Inc, Irvine, California, USA) have been shown to be effective in treating uveitis in both adults and children, with effects lasting up to 6 months following a single implantation.[12–14] This allows for less frequent implantations, which further reduces the risk of procedure-related adverse events, as well as a good safety profile, with few patients having cataract progression or increased intraocular pressure, compared to other regional corticosteroid injections.[15] While the effect of a single implant has been reported, the effect of repeat treatment using dexamethasone implants on disease control, visual function, and the use of systemic medications has not yet been explored.

In this study we examined the outcome of repeat intravitreal dexamethasone implants for the treatment of uveitis in children. We examined the cumulative effect of using repeat dexamethasone implantations on clinical outcome, systemic treatment, and complication rates.

METHODS

• PATIENT SELECTION: This is a retrospective study of patients seen at Moorfields Eye Hospital, London, UK

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(ethical approval for data collection LIGS10201, visual loss in uveitis, Moorfields Eye Hospital research and development ethics review board). The study adhered to the tenets of the Declaration of Helsinki. The study included all pediatric noninfectious uveitis patients seen between the years 2008–2014 who were given an intravitreal dexamethasone implant. Patients were offered treatment with a dexamethasone implant if they had previously responded to a local corticosteroid injection but needed short-term repeated treatments, or when systemic treatment was not well tolerated or was ineffective at low doses. All implantations were performed under general anesthesia, as per national regulations, and were uneventful. Repeat implantations were performed in cases when patients were intolerant to systemic immunosuppression or systemic side effects, such as growth retardation, delayed puberty, and weight gain, clinically outweighed the anesthetic risks. All patients were managed under the care of a single consultant (S.L.). Treatment decisions were determined based on vision, clinical evaluation of active inflammation or presence of CME, response to systemic treatment, and side effects. Following implantation, systemic treatment was reduced with an aim to stop all systemic drugs. The decision to repeat treatment with a dexamethasone implant was based on return of CME on optical coherence tomography (OCT; Spectralis, Heidelberg Engineering, Heidelberg, Germany); a further decrease in visual acuity related to recurrent vitritis, as noted on biomicroscopy; or more than a doubling of the angle of best-corrected visual acuity (BCVA).

• **DATA COLLECTION:** Information for each patient was collected according to the length of follow-up, on the day of implantation; at months 1, 2, 3, 6, 12, 18, and 24; and at the patient's last follow-up visit. From each visit information was recorded including BCVA, central retinal thickness (CRT), intraocular pressure (IOP), and vitreous haze score (range 0–4). BCVA results were converted to logarithm of the minimal angle of resolution (logMAR) for statistical analysis and are presented as logMAR and Snellen equivalent. Furthermore, numbers of topical drugs used for treating inflammation or elevated IOP, as well as systemic and regional corticosteroids and immunosuppressive drugs, were recorded. Postimplantation complications, if occurred, were noted, including development of cataract, raised IOP above 21 mm Hg, migration of implants into the anterior chamber, endophthalmitis, and retinal detachment. Record was made of any treatments that were required to address such complications.

• **STATISTICAL ANALYSIS:** Change in mean BCVA and CRT was compared to the time of each injection using the generalized estimating equation, adjusting for correlation between 2 treated eyes of the same patient and using the Bonferroni correction for multiple tests. Change of BCVA following repeat implantations was calculated using the Spearman correlation. The Pearson χ^2 test was used to analyze the proportion of patients achieving a vitreous score of 0. The Kaplan-Meier estimator was used to examine survival from relapse. SPSS (version 22; SPSS Inc, Chicago, Illinois, USA) was used for all analyses. The accepted level of significance for all tests was $\alpha \leq 0.05$. Continuous data are presented as means ± standard error of the mean (SEM).

TABLE. Baseline Characteristics for Eyes With Pediatric Uveitis Before Beginning Treatment With Dexamethasone Implants

Baseline Eye Characteristics	N (%)
Eyes	22
Duration of uveitis, mo, mean (SEM)	44.25 (6.26)
Diagnosis	
Intermediate uveitis	14 (63.6)
Posterior + panuveitis	8 (36.4)
Reason for treatment	
CME	17 (77.3)
Vitritis	5 (22.7)
Baseline visual acuity, logMAR, mean (SEM)	0.55 (0.08)
Severity of vitreous haze at baseline	
Score of 0	9 (40.9)
Score of +0.5 to +3	13 (59.1)
Baseline central retinal thickness, μm, mean (SEM)	438.07 (41.85)
Baseline intraocular pressure, mm Hg, mean (SEM)	12.55 (1.01)
Phakic, clear lens at baseline	11 (50)
Steroid responders at baseline	10 (45.5)
Repeat implants	
2 implants	6 (27.3)
3 implants	2 (9.1)
4 implants	1 (4.5)

CME = cystoid macular edema; LogMAR= logarithm of the minimal angle of resolution; SEM = standard error of mean.
Most eyes required ozurdex implantations to treat CME.

RESULTS

TWENTY-TWO EYES OF 16 PATIENTS (9 MALE, 7 FEMALE) WERE included in this study (Table). Eyes were diagnosed as having either intermediate uveitis (n = 14) or posterior/panuveitis (n = 8). Etiologies included Vogt-Koyanagi-Harada syndrome (n = 2), juvenile idiopathic arthritis (n = 2), pars planitis (n = 3), and idiopathic (n = 15). Average age at the time of the first implantation was 13 ± 0.7 years (range 9.5–17 years). At the time of the first implantation (baseline) 9 patients were being treated with systemic prednisolone at an average dose of 26 ± 4 mg. Eleven patients had previously received steroid-sparing agents (8 mycophenolate mofetil, 3 infliximab, 2 azathioprine, 2 methotrexate, 1 cyclosporin), of which 4 were still being