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Journal
Ophthalmology Retina, 3(11)

ISSN
2468-7219

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Publication Date
2019-11-01

DOI
10.1016/j.oret.2019.05.030

Peer reviewed

Published in final edited form as:

Ophthalmol Retina. 2019 November ; 3(11): 993–997. doi:10.1016/j.oret.2019.05.030.

Dexamethasone intravitreal implant injection in eyes with comorbid hypotony

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Abstract

Purpose: To evaluate outcomes in patients with hypotony treated with intravitreal dexamethasone implant (Ozurdex).

Design: Retrospective cohort study

Participants: 15 eyes of 13 patients that received a total of 99 dexamethasone implant injections on occasions at which the intraocular pressure was low, meeting the definition of statistical hypotony.

Methods: The medical records of 13 patients (15 consecutive eyes) receiving ≥1 intravitreal dexamethasone implants between December 2014 and April 2017 were reviewed retrospectively. Hypotony was defined as intraocular pressure < 6.5 mmHg. The indications for intravitreal dexamethasone implant injection were intermediate or posterior uveitis (86.7%), diabetic macular edema (13.3%), and cystoid macular edema (6.7%).

Main Outcome Measures: The primary outcome measures were safety outcomes and best visual acuity within six months of final intravitreal dexamethasone implant injection in a hypotonous eye.

Results: In 15 eyes (13 patients), 99 injections were administered to eyes under circumstances of hypotony. Uveitic cystoid macular edema or diabetic macular edema was reduced following treatment in all cases. No complications were noted during the injection procedure. Three complications were noted in two patients after injection. Pseudo-phakodonesis and mild vitreous hemorrhage immediately following injection were noted in one patient, and a case of delayed onset vitreous hemorrhage with pigment release was noted in another. All three complications resolved without intervention. The primary endpoint of this study, mean visual acuity, was stable over the follow-up period. In hypotonous patients whose intraocular pressure normalized during

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Conflict of interest: The authors declare no conflict of interest.

the follow-up period, this was attributable to management of glaucoma-surgery related complications rather than an effect of the intravitreal dexamethasone implant.

Conclusion: Intravitreal dexamethasone implant injection is a reasonable treatment option for patients with comorbid hypotony in whom clinical findings warrant treatment with a sustained-delivery intravitreal steroid implant. Further studies, including imaging of zonules before and after intravitreal dexamethasone implant injection in a hypotonous eye, could help define risks to intraocular lens stability with this procedure.

Introduction

The dexamethasone intravitreal implant (Ozurdex) is widely used in treating inflammatory disease, such as uveitis, as well as other conditions involving macular exudation. The implant provides a sustained release of the corticosteroid dexamethasone for six months and degrades on its own without surgical removal.[1] The efficacy of the intravitreal dexamethasone implant in uveitis and other indications has been proven in clinical trials[1–3], and the majority of reports have shown that intravitreal dexamethasone implant injection is a safe procedure.[4,5]

Hypotony, a condition in which the intraocular pressure (IOP) is lower than normal, can occur as a complication of chronic uveitis or other causes such as trauma or surgery. In a randomized study of 255 uveitis patients, 8.3% also had hypotony.[6] Choroidal thickening and folding related to hypotony can be risk factors for complications associated with intraocular procedures due to an increased risk of the needle tip engaging the choroidal tissue as it is introduced into the eye. One case of choroidal detachment due to complications from hypotony after intravitreal injection of the dexamethasone implant has been reported.[7] The intravitreal dexamethasone implant injection could be considered to be a higher risk procedure than other intravitreal injections such as anti-vascular endothelial growth factor (anti-VEGF) due to the larger needle gauge required for injection of the implant (22g needle, versus 30g for most other intravitreal pharmacologic agents). In a study evaluating 25g trocar insertion, Rizzo et al[8] speculated that the extra force needed to penetrate the sclera in eyes with hypotony can cause traumatic ciliochoroidal detachment at the sclerotomy site. If the intravitreal dexamethasone implant injection were to cause ciliochoroidal detachment, it could aggravate the hypotony and further increase the risk of the injection.[9,10] Therefore it is unclear whether it is reasonable to offer the intravitreal dexamethasone implant treatment in patents with hypotony. We conducted this study to evaluate outcomes in patients with hypotony treated with the intravitreal dexamethasone implant.

Methods

This was a retrospective, consecutive study. The study was approved by the Human Research Protection Program (HRPP) at the University of California, San Francisco (UCSF), and this research adhered to the tenets of the Declaration of Helsinki. The UCSF HRPP granted a waiver of consent statement affirming that patient welfare would not be adversely affected by waiving informed consent. All patients who underwent an intravitreal dexamethasone implant injection in an eye with hypotony (IOP <6.5 mmHg)[11] with a retina

specialist at the University of California, San Francisco, between December 2014 and April 2017 were included, regardless of the indication for treatment. IOP was measured immediately before injection procedure between 8AM and 5PM. These patients were then followed through October 31, 2018.

A standard injection procedure was followed. After topical anesthesia and povidone-iodine application as well as subconjunctival anesthesia, an eyelid speculum was placed, and intravitreal injection of the intravitreal dexamethasone implant was performed 3.5 to 4 mm posterior to the limbus. In cases in which low IOP made it more difficult for the needle tip to enter the globe, applying a more tangential insertion angle, parallel to the limbus, facilitated penetration of the sclera.

Data on IOP, visual acuity (VA), and complications were collected for each patient at each follow-up visit. All eyes were evaluated for lens position or pseudophakodonesis. For patients with macular edema, data on central macular thickness was also collected. Because effects of the dexamethasone intravitreal implant may last as long as six months[1], the primary endpoint of this study was defined as best visual acuity within six months of final implant injection in a low IOP eye. Spectral-domain optical coherence tomography (SD-OCT) was also performed for each patient at every follow-up appointment. VA, IOP, and macular SD-OCT were then compared with the previous visit.

Stata 15.0 and Microsoft Excel were used for data analysis. All visual acuity measurements were converted to logMAR and ETDRS letters.[12–14] A paired two-tailed *t*-test was used for changes in VA and IOP between the first injection in a low IOP eye and six-months post final low IOP injection.

Results

Thirteen consecutive patients (15 eyes) were included in the study. All had at least one occasion on which hypotony was present (IOP less than 6.5 mm Hg) at the time of the intravitreal dexamethasone implant injection. The follow-up period for each patient began at the time of first dexamethasone intravitreal implant injection in a low IOP eye. In 11 eyes, prior glaucoma surgery had been performed, and in all of these eyes the hypotony was attributable to the pressure-lowering effects of that surgery; in the other 4 eyes, the hypotony was due to complications of uveitis. Patient characteristics at the time of the first low pressure injection visits are listed in Table 1.

The median number of injections in eyes with low pressure was 5, and the median duration of follow-up was 25.4 months (Table 2). The total number of occurrences of the intravitreal dexamethasone implant injection into eyes under hypotonous conditions was 99. Total number of injections during the study period regardless of eye pressure was 141.

With regards to vision, the mean visual acuity was 20/126 at the first visit, and improved to 20/95 at best within six months post final injection in a low IOP eye (P=0.05, Table 3). Mean IOP was 4.27 mm Hg at the first visit, and this increased to8.0 mm Hg at the final visit, and this change was statistically significant (P=0.03). In 13 eyes (86.7%), 10 of which had prior glaucoma surgery, IOP increased from a hypotonous measurement at baseline to a normal or

high reading at the final visit. The median number of the intravitreal dexamethasone implant injections in eyes whose IOP increased by the final visit was 4 (range 1–20). In 2 eyes (13.3%), IOP remained hypotonous from the first through the final visit. In these eyes, the number of injections was 9 for both eyes. Regardless of IOP changes, primary uveitis or diabetes treatment outcomes such as reduction in macular edema were achieved in all cases.

Three complications were observed in two patients after the procedure. In a 75-year-old woman with intermediate uveitis and cystoid macular edema, some movement of the intraocular lens during saccades was observed after the 10th intravitreal dexamethasone implant injection performed while the eye was hypotonous. Four injections later, hyphema and mild vitreous hemorrhage were noted immediately following the injection procedure. This occurred in the absence of any neovascularization or anti-coagulant use and correlated with bleeding visualized externally at the injection site, which was tamponaded with digital pressure. In this case, there was no clinically significant change in lens position, and the hyphema and vitreous hemorrhage resolved without intervention within a month.

The third complication was a case of vitreous hemorrhage with pigment release five days after the 13th injection in a low IOP eye, in an 82 year-old man with cystoid macular edema and a history of vitrectomy for endophthalmitis. Upon examination at the time of symptom onset, mild vitreous hemorrhage and pigmented vitreous cells were present, but no retinal tears or retinal or preretinal hemorrhages were noted. The patient did not report any pain and was advised to limit physical activity until the vitreous hemorrhage resolved on its own. This occurred in a vitrectomized eye in which the intravitreal dexamethasone implants were routinely noted to be mobile by both the patient and the physician, and it was hypothesized that the intravitreal dexamethasone implant had moved into a location where it was able to chafe against pigmented tissue, causing release of blood and pigmented cells. This complication was not felt to be related specifically to hypotony in this eye.

Discussion

To the best of our knowledge, this is the first report on the clinical experience of using the dexamethasone intravitreal implant injection for patients with comorbid ocular hypotony. Previous studies have examined IOP immediately after and during the twelve months post dexamethasone intravitreal implant injection in non-hypotonous eyes[15,16]. In this series, the procedure was well-tolerated, suggesting that this treatment option may be considered for management of various ophthalmic conditions despite low IOP, if warranted by clinical circumstances.

We also found that the VA and IOP on average increased during the follow-up period—twelve of the patients had stable or improved vision, and eleven patients had stable or elevated IOP. This indicates that the intravitreal dexamethasone implant treatment was able to meet clinical endpoints[17–19] despite the hypotony.

Unforeseen complications resulting from the technical challenge of performing the injection in hypotonous eyes are a potential concern. In one of our cases, a patient was found to have an unstable-appearing intraocular lens during the follow-up period. It is not clear whether

this was a result of the injection procedure, but it seems possible that distortion of the ciliary sulcus and pars plana region during injection in a soft eye could stretch or rupture zonules. Nevertheless, no IOL dislocation or vision-affecting position change was noted in this study. Further studies, including high-resolution imaging of zonules before and after the intravitreal dexamethasone implant injection in a hypotonous eye, could help better define the risks to IOL stability with this procedure.

One of the eyes that experienced post-injection complications had histories of vitrectomies. This might suggest that history of vitrectomy may be a risk factor for post-injection complications in eyes with low pressure, possibly by making it easier for the globe shape to be distorted during the injection.

Ten of the eleven hypotonous eyes whose IOP increased after intravitreal dexamethasone implant injection were in eyes with previous glaucoma surgery. In these cases, restoration of a higher, more normal pressure occurred in the course of management of the surgically-induced hypotony, such as by correction of an overfiltering bleb. Therefore the results of this study do not support that intravitreal dexamethasone implant injection alone increased IOP in these hypotonous eyes.

Finally, although it is reassuring that no choroidal detachment or worsening of hypotony was noted in this series, these potential complications should be considered when offering intravitreal dexamethasone implant injection to patients with hypotony. Increasing the pressure of hypotonous eyes with a balanced salt solution-injection with a small-guage needle prior to implant injection may also increase safety[20]. Based on our experience with this group of patients, though, the intravitreal dexamethasone implant appears to be a reasonable option for patients with hypotony in whom treatment is indicated by clinical findings.

Financial support:

National Eye Institute (NIH-NEI 1R01EY024004 and NIH-NEI, EY002162 Core Grant for Vision Research), Research to Prevent Blindness, and, That Man May See, Inc.

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Table 1:

Baseline characteristics

Age (years)	
Mean	60.1
Median	66
Range	36–83
Female sex: n, (%)	8 (53.3)
Diagnosis (n, eyes)	
Intermediate or posterior uveitis	13
Diabetic macular edema	2
Cystoid macular edema	1
Prior cataract surgery: n, eyes (%)	14 (93.3)
Prior glaucoma surgery: n, eyes (%)	11 (73.3)
Hypotony attributable to prior glaucoma surgery: n, eyes (%)	11 (73.3)
Prior vitrectomy surgery: n, eyes (%)	4 (26.7)

Table 2:

Procedures and follow-up

Number of injections, total	
Overall	141
Eyes with low IOP	99
Number of injections per eye, low pressure	
Mean	6.6
Median	5
Range	1–20
Number of injections per eye, total	
Mean	9
Median	9
Range	1–24
Follow-up (months), from time of first low IOP injection	
Mean	27.3
Median	25.4
Range	1.6–55.5
IOP (mmHg), all injection visits	
Mean	6.8
Median	6
Range	0–23
IOP (mmHg) at time of injection, considering only visits with hypotony	
Mean	4.4
Median	5
Range	0–6.0

Table 3:

Visual acuity changes from baseline

Eye	BL, Snellen	BL, ETDRS Letters	6M Post Final Low IOP Injection, Snellen	6M Post Final Low IOP Injection, ETDRS Letters
1	20/70	72.8	20/70	76.1
2	20/70	72.8	20/60	76.1
3	20/250	0.0	20/200	50.0
4	20/50	80.1	20/25	95.2
5	20/50	80.1	20/70	72.8
6	20/150	56.2	20/125	60.2
7	20/100	65.1	20/70	72.8
8	20/2000	0.0	20/2000	0.0
9	20/40	84.9	20/40	84.9
10	20/50	80.1	20/25	95.2
11	20/200	50.0	20/40	84.9
12	20/200	50.0	20/200	50.0
13	20/400	34.9	20/630	25.1
14	20/125	60.2	20/100	65.1
15	20/100	65.1	20/20	100.0
Mean (+/−SD)	20/126	59.8 +/− 26.0	20/95	67.0 +/− 27.2
p-value (vs. BL)	0.05			

BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study; 6M, 6 months; IOP, intraocular pressure; SD, standard deviation

When clinically indicated, the dexamethasone intravitreal implant (Ozurdex) can be administered in hypotonous eyes, with a low rate of complications.