

## SCIENTIFIC REPORT

## Trans-Tenon's retrobulbar triamcinolone infusion for the treatment of uveitis

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**Aim:** To assess efficacy and complications of trans-Tenon's retrobulbar infusion of triamcinolone acetate for posterior uveitic inflammation.

**Methods:** Non-randomised, uncontrolled, retrospective study of 51 eyes of 37 patients who underwent triamcinolone infusion for vitritis, cystoid macular oedema (CMO), or posterior retinal vasculitis using a long blunt cannula via an incision made through conjunctiva and Tenon's capsule.

**Results:** Overall clinical efficacy was 86%; 96% for vitritis, 82% for CMO, and 33% for posterior retinal vasculitis. Mean visual acuity improved within 1 month after triamcinolone infusion ( $p < 0.05$ ). Cataract progression and intraocular pressure elevation were observed in 31% and 27% of eyes, respectively.

**Conclusion:** Trans-Tenon's retrobulbar triamcinolone infusion may be a safe and effective treatment for posterior uveitic inflammation.

Periocular injections of long acting corticosteroids have been used to deliver high drug concentrations to the posterior eye for cystoid macular oedema (CMO) and other posterior segment inflammatory changes associated with uveitis. Several techniques have been advocated including subconjunctival, sub-Tenon's capsule, trans-septal, orbital floor, and retrobulbar injections<sup>1-6</sup>; however, the success of each technique has been limited and each technique is associated with various complications caused by the injection itself, including blepharoptosis, orbital fat herniation, globe perforation, and even retinal and choroidal vascular occlusion.<sup>1-9</sup> More recently, intravitreal corticosteroid injections<sup>10-12</sup> and intravitreal corticosteroid implants<sup>13-14</sup> have also been investigated; however, these methods carry the risk of complications associated with such intravitreal procedures including vitreous haemorrhage, retinal detachment, suprachoroidal placement of implant, and endophthalmitis.<sup>13-15-16</sup>

We have utilised a trans-Tenon's retrobulbar infusion of triamcinolone to treat CMO and acute posterior segment inflammation associated with uveitis. This technique is most similar to the "limbal sub-Tenon's administration of retrobulbar anaesthesia using a blunt irrigating cannula" reported by Bergman and colleagues.<sup>17</sup> A letter by Sajani suggests this technique for delivering corticosteroid,<sup>18</sup> but does not give any data on efficacy in uveitis. Our technique differs from previously reported sub-Tenon's injections in uveitis in that (1) it does not involve a sharp needle, (2) the cannula used is long and able to reach behind the posterior globe, and (3) cannula entry into sub-Tenon's space is confirmed visually. The space beneath Tenon's capsule around the anterior globe is continuous with the space beneath the visceral layer of dura surrounding the optic nerve and is equivalent to the retrobulbar space.<sup>19</sup> Therefore, we have named our technique "trans-Tenon's retrobulbar infusion."

## PATIENTS AND METHODS

Trans-Tenon's retrobulbar triamcinolone infusion was performed in 51 consecutive eyes of 37 patients with uveitis (21 women, 16 men) for vitritis (26 eyes), CMO (22 eyes), or retinal vasculitis involving the posterior pole (three eyes), not improving with topical corticosteroids. Patients had the following diagnoses: sarcoidosis, eight patients (11 eyes); Behçet's disease, eight patients (11 eyes), Vogt-Koyanagi-Harada (VKH) disease, six patients (12 eyes); tuberculous uveitis, three patients (three eyes); serpiginous choroiditis, one patient (two eyes); acute anterior uveitis (AAU), one patient (one eye); sclerouveitis, one patient (one eye); unknown aetiology, nine patients (10 eyes). Seven patients with Behçet's disease were taking concurrent systemic colchicine and/or cyclosporin. The three patients with tuberculous uveitis were taking concurrent systemic isoniazid and rifampin, started at least 1 month before triamcinolone infusion. Nine other patients (VKH disease, four patients; sarcoidosis, two patients; AAU, one patient; serpiginous choroiditis, one patient; panuveitis of unknown aetiology, one patient) were concurrently receiving systemic corticosteroids and/or cyclosporin. The systemic regimen was either unchanged or in the process of being tapered over the first 3 months after initial triamcinolone infusion in all patients. Median patient age was 55 years (range 19-81 years) and median post-triamcinolone infusion follow up period was 13 months (range 4-29 months). Clinical records were reviewed retrospectively and did not require institutional review board approval.

Informed consent was obtained before each procedure. The patient's eye was prepared with 0.3125% povidone-iodine and draped in a minor procedure room. A lid speculum was placed after topical instillation of 0.4% oxybuprocaine or 4% Xylocaine. Under a 5× operating microscope, conjunctiva and Tenon's capsule were incised in the inferotemporal quadrant, approximately 3-4 mm posterior to the limbus using smooth microforceps and conjunctival scissors, just enough to create a small buttonhole opening through to bare sclera. Next, a 23 gauge curved blunt cannula approximately 2.1 cm in length (#HS-2764, Handaya Co, Ltd, Tokyo, Japan) was introduced through this opening and inserted to the hub. If resistance was met, the cannula was pulled back and reinserted to ensure smooth movement through the plane between Tenon's capsule and sclera. Once in position, and after confirmation that no fluid entered the syringe upon attempted aspiration, 0.5 ml of 40 mg/ml (total dose 20 mg) triamcinolone acetate (Bristol Pharmaceutical, KK, Tokyo, Japan) was infused using a 1 ml tuberculin syringe. If any resistance was met during infusion, the cannula was withdrawn slightly and infusion reattempted, allowing for proper infusion without reflux through the wound opening. The procedure was associated with mild discomfort in some patients but no frank pain. At the end of the procedure, the wound was left unsutured and 0.5% levofloxacin was instilled into the eye. The patient was instructed to use 0.5% levofloxacin eye drops three times a day for 1 week.

**Table 1** Efficacy of trans-Tenon's retrobulbar triamcinolone infusion in uveitis (numbers are number of eyes (%))

	Efficacy assessed by: funduscopy*	FA*	OCT*	Visual acuity improvement†
Vitritis (n = 26)	25/26 (96)	NA	NA	11/14 (79)
Cystoid macular oedema (n = 22)	18/22 (82)	4/5 (80)	12/15 (80)	11/16 (69)
Posterior retinal vasculitis (n = 3)	1/3 (33)	1/1 (100)	NA	0/1 (0)
Total	44/51 (86)			22/31 (71)

\*Denominator represents number of eyes in which the examination was performed both before and within 3 months after initial triamcinolone infusion, and numerator represents eyes that showed improvement. Improvement by funduscopy for vitritis was defined as decrease in the vitreous haze score (published scale 1–5).<sup>20</sup> For cystoid macular oedema (CMO), funduscopy improvement was defined as resolution of intraretinal cysts. For retinal vasculitis, funduscopy improvement was defined as at least 50% decreased haemorrhages and exudates along inflamed vessels. Improvement by FA for CMO was defined as decreased pooling in late images of the fovea (arbitrary scale 1–4), and for retinal vasculitis as decreased vascular leakage or staining (arbitrary scale 1–4) in late images. Improvement by OCT for CMO was defined as at least 50% decreased height of retinal thickness in the center of the fovea and return of the normal foveal configuration.

†Denominator represents eyes with a best corrected visual acuity of 0.155 logMAR or worse at the time of initial triamcinolone infusion, and numerator represents eyes in this group that had a 0.200 logMAR or greater visual acuity improvement within 3 months.  
FA = fluorescein angiography; OCT = optical coherence tomography; NA = not applicable.

Patients were examined by slit lamp biomicroscopy and binocular indirect funduscopy at least once a month after triamcinolone infusion, and efficacy was defined as improvement in severity of the finding within 3 months. Fluorescein angiography (FA) and/or optical coherence tomography (OCT) were performed at the attending physician's discretion in some but not all eyes. Cataract progression was assessed clinically by slit lamp biomicroscopy throughout the follow up period, and was defined as new or increase in any type of lens opacification after triamcinolone infusion (arbitrary scale 1–4). Intraocular pressure (IOP) elevation was defined as an IOP greater than 22 mm Hg by applanation tonometry. Repeat triamcinolone infusion was considered *only* in the absence of elevated IOP and in most cases after at least 3 months had passed since the previous infusion.

## RESULTS

The overall efficacy rate after initial trans-Tenon's retrobulbar triamcinolone infusion was 86% for all 51 eyes (Table 1). Efficacy by funduscopy was 96% for vitritis, 82% for CMO, and 33% for retinal vasculitis. Efficacy in the latter two groups was supported by FA and/or OCT performed in some but not all eyes.

Visual acuity improvement after initial triamcinolone infusion was assessed for those eyes in each group with a pretreatment visual acuity of 0.155 logMAR or worse (Table 1). A 0.200 logMAR or greater visual acuity improvement within 3 months was documented in 79% for vitritis, 69% for CMO, and 0% for retinal vasculitis. The median visual acuity of all eyes improved from 0.222 logMAR (range 2.000 to –0.079 logMAR) before treatment, to 0 logMAR (range 1.301 to –0.079 logMAR) at 1 month, and 0 logMAR (range 1.222 to –0.079 logMAR) at 3 months. The mean visual acuity of all eyes improved from 0.380 logMAR before treatment, to 0.170 logMAR at 1 month, and 0.160 logMAR at 3 months (both  $p < 0.05$ , paired  $t$  test). Only one eye lost 0.200 logMAR or greater visual acuity within 3 months after triamcinolone infusion. This eye was in a patient with choroiditis of unknown aetiology and CMO. The visual acuity decreased from 0.155 logMAR pre-triamcinolone infusion to 0.699 logMAR at 2 months because of the onset of subretinal fluid in the fovea as confirmed by OCT. The subretinal fluid resolved completely within 3 months, and after 39 months of further follow up the visual acuity has remained stable at 0.523 logMAR with no active inflammation but with mild pigmentary changes in the fovea.

The majority of eyes (32 eyes, 63%) received only one triamcinolone infusion. However, over the entire follow up period, nine eyes (18%) received two infusions, four eyes (8%) three infusions, three eyes (6%) four infusions, two eyes (4%) five infusions, and one eye (2%) seven infusions. Five eyes

underwent repeat triamcinolone infusion at the same dose at 2–4 weeks after the initial infusion because of a clinically inadequate or slow response, while 14 eyes underwent repeat triamcinolone infusion for episodes of recurrent inflammation separate from that treated by previous infusions.

Cataract progression occurred in 16 eyes (31%, Table 2) and IOP elevation occurred in 14 eyes (27%). IOP elevation occurred after the initial triamcinolone infusion in 10 eyes and after a subsequent infusion in four eyes. IOP elevation developed at 2–3 months after treatment in all cases and was controlled using a single topical antiglaucoma medication that could be discontinued by 6 months after the procedure in 13 eyes. No disc cupping or visual field loss was observed in these 13 eyes. One eye in a patient with Behçet's disease developed refractory IOP elevation and eventually underwent filtration surgery. This patient was taking concurrent oral corticosteroids and cyclosporin, and the eye with the IOP elevation had received a total of seven triamcinolone infusions for separate recurrences of inflammation over a 2 year period and the patient was taking topical corticosteroids. The eye was documented to have an open angle, no disc cupping, and a normal Goldmann visual field both before and after filtration surgery.

Mild subconjunctival haemorrhage was occasionally associated with the triamcinolone infusion; however, there were no cases of blepharoptosis, retrobulbar haemorrhage, globe perforation, infection, vascular occlusion, or systemic complications observed.

**Table 2** Rates of cataract progression and intraocular pressure elevation (numbers are number of eyes (%) (n = 51 eyes))

Cataract progression*	
Total	16 (31)
Eyes receiving more than one triamcinolone infusion	9 (18)
Eyes receiving concomitant corticosteroid eyedrops	14 (27)
Eyes in patients receiving concomitant oral corticosteroids	1 (2)
Eyes that underwent cataract surgery	3 (6)
Intraocular pressure elevation†	
Total	14 (27)
Eyes receiving more than one triamcinolone infusion	6 (12)
Eyes receiving concomitant corticosteroid eyedrops	11 (22)
Eyes in patients receiving concomitant oral corticosteroids	3 (6)
Eyes that underwent filtration surgery	1 (2)

\*Cataract progression was assessed by slit lamp biomicroscopy throughout the follow up period and was defined as new or increase in any type of lens opacification after triamcinolone infusion (arbitrary scale 1–4).

†Intraocular pressure (IOP) elevation was defined as an IOP greater than 22 mm Hg by applanation tonometry. All eyes with IOP elevation were successfully treated with topical antiglaucoma medications, except for one eye in a patient with Behçet's disease that eventually underwent filtration surgery.

## DISCUSSION

The present study evaluates the results of trans-Tenon's retrobulbar triamcinolone infusion for uveitic eyes, using a long blunt cannula after incision of conjunctiva and Tenon's capsule. For comparison, Yoshikawa, *et al* used posterior sub-Tenon's injections of 25–50 mg triamcinolone via a 1.9 cm needle in 39 uveitic eyes with CMO and found a two line or greater visual acuity improvement in 56.4% of eyes.<sup>3</sup> Helm and Holland reported that posterior sub-Tenon's injection of 40 mg triamcinolone using a 5/8 inch needle produced a two line or greater visual acuity improvement in 12 of 18 eyes (67%) with CMO associated with intermediate uveitis.<sup>4</sup> Tanner *et al* utilised 40 mg triamcinolone sub-Tenon's injections via a 5/8 inch needle in 28 eyes for CMO associated with posterior or intermediate uveitis,<sup>6</sup> and found a two line increase in visual acuity in 40% of eyes at 12 weeks post-injection and a decrease in the mean vitreous cell score for 18 patients. These reports lack data on efficacy by FA or OCT, and do not evaluate efficacy in vitritis or retinal vasculitis. Furthermore, differences in visual acuity measurement and definition of visual acuity improvement make direct comparison with the present study difficult. However, for uveitic CMO, we believe that our results with trans-Tenon's retrobulbar infusion are comparable if not better, particularly since only 20 mg of triamcinolone was used. In addition, 80% of CMO eyes that underwent pre-triamcinolone and post-triamcinolone infusion FA or OCT showed objective improvement (Table 1), further supporting the high efficacy rate of this method.

Magnetic resonance imaging (MRI) in eyes receiving preoperative ocular anaesthesia using a technique similar to that in this study shows that drug is reliably deposited into the retrobulbar space.<sup>19</sup> A similar retrobulbar location of corticosteroid was documented by B-mode ultrasonography in 15 of 16 eyes given retrobulbar injections for inflammatory CMO.<sup>21</sup> In contrast, only 17 of 24 eyes (71%) with inflammatory CMO given a sub-Tenon's injection of corticosteroid using a 5/8 inch needle were found to have the bolus of medication posterior to the equator by B-mode ultrasonography.<sup>22</sup> Of the remaining eyes, six were found to have the drug deposited into the orbit while one eye was found to have the drug deposited in the vicinity of the equator. Ultrasonography and MRI were not used to confirm drug location in the present study. However, since trans-Tenon's retrobulbar infusion involves visual confirmation of cannula entry into sub-Tenon's space, we believe that reliable drug placement using this method contributes to a high rate of efficacy.

Trans-Tenon's retrobulbar infusion in the current study was associated with few complications because of the technique itself. Potential complications may include conjunctival abscess, retrobulbar haemorrhage, orbital cellulitis, and globe perforation. Greater numbers of eyes examined in a prospective fashion would be necessary to further delineate safety.

It is not clear whether rates of cataract progression and IOP elevation differ between trans-Tenon's retrobulbar infusion and posterior sub-Tenon's injection of triamcinolone. In this study, rates for cataract progression and IOP elevation were 31% and 27%, respectively. Most of these eyes were receiving concomitant topical corticosteroids. One eye in our study eventually underwent filtration surgery for refractory glaucoma. For comparison, cataract progression was observed in six of 39 eyes (15%) after posterior sub-Tenon's injections of corticosteroid in the study by Yoshikawa *et al* although the follow up period was not indicated.<sup>3</sup> Their study also reported that filtration surgery was necessary in one eye, although overall rate of IOP elevation was not given. Helm and Holland reported IOP elevation in six of 20 eyes (30%) in patients receiving posterior sub-Tenon's injections of triamcinolone over a follow up period of 1 to 50 months (median 23.5 months).<sup>4</sup> During this period of time, the number of eyes with cataract increased from nine (45%) to 13 (65%).

There has been much recent interest in the use of intravitreal corticosteroid injections<sup>10–12</sup> and intravitreal corticosteroid implants<sup>13–14</sup> for the treatment of uveitis. Intravitreal injection of 2 mg triamcinolone was reportedly effective in five of six eyes with uveitic CMO in one study, although one eye required trabeculectomy for persistent IOP elevation.<sup>10</sup> A separate study using 4 mg triamcinolone injected intravitreally reported reduced uveitic CMO in six of six eyes, although five eyes developed IOP elevation to 30 mm Hg or greater and two eyes developed cataract.<sup>12</sup> One other study reported efficacy in two of two eyes with refractory CMO associated with birdshot retinochoroidopathy using an intravitreal injection of 4 mg triamcinolone.<sup>11</sup> Intravitreal implants are still being evaluated in clinical trials. All intravitreal techniques for depositing corticosteroid are inherently associated with risks of intraocular complications because of the injection or implantation technique, not to mention possibly higher rates of cataract progression and IOP elevation. Therefore, we believe it preferable to perform the trans-Tenon's retrobulbar triamcinolone infusion as described in this study before considering a globe invasive injection or implant of the same or similar corticosteroid in eyes already compromised with uveitis.

However, a clear disadvantage of this triamcinolone infusion technique compared to sub-Tenon's or periorbital injection is that it cannot be performed at the slit lamp or with the patient sitting upright in an examination room. A minor procedure area and post-treatment topical antibiotics are required. Furthermore, compared to intravitreal corticosteroid implants, the corticosteroid effect of the triamcinolone infusion or any periorbital or intravitreal injection lasts much shorter, necessitating repeat treatments in some eyes. Such differences need to be considered in tandem with consideration of the type of disease being treated (some problems require longer exposure to the corticosteroid effect) and ability of the patient to cooperate with a procedure when deciding between trans-Tenon's retrobulbar triamcinolone infusion and other techniques for placing corticosteroid in or around the eye.

In summary, this non-randomised, uncontrolled, retrospective study found trans-Tenon's retrobulbar triamcinolone infusion to be effective in reducing posterior inflammation in uveitis, particularly in eyes with vitritis or CMO. Although cataract progression and IOP elevation were observed, complications associated with sub-Tenon's injections using needles such as blepharoptosis and globe perforation were not noted. We conclude that trans-Tenon's retrobulbar triamcinolone infusion may be a safe and effective treatment for posterior inflammation in uveitic eyes.

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