The Use of Intravitreal Triamcinolone Acetonide – An Overview

a report by
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Triamcinolone acetonide is an intermediate-acting, relatively powerful steroid (see *Table 1*). Like all steroids, it dampens both the cell-mediated and the humoral component of inflammatory reactions. Clinically, this translates to reduced vessel permeability, justifying the use of this drug in most cases of macular oedema. It has also been shown to block the breakdown of the blood–ocular barrier by modulating effector proteins downstream of the vessel growth factor (VEGF) receptor.[1] Triamcinolone acetonide has been shown to be present in the vitreous up to three months after delivery.[2] It should be kept in mind that this is true only for non-vitrectomised eyes; in eyes that have been vitrectomised the drug is present for much shorter periods of time after delivery and is, to some extent, related to the amount of vitreous still present. The use of intravitreal triamcinolone acetonide (IVT) has given ophthalmologists new treatment options in a variety of ocular ailments, as demonstrated by the large number of papers and reports on this topic that are now available. This is not surprising, as IVT is the solution to many retinal conditions in which potent and localised suppression of the inflammatory cascade is needed. However, there are indications, limitations and side effects to the use of the drug that must be considered in clinical practice.

Clinical Applications

Uveitis

Chronic non-infective uveitis (CNU) should be approached as a systemic disease with the eye as the predominant target. As such, systemic therapy with steroids and/or other immunosuppressive agents is generally the rule.[3] Severe cases of CNU are almost invariably associated with macular oedema. Cases of controlled uveitis in which macular oedema is responsible for visual acuity (VA) deterioration can benefit from IVT.[4] The use of IVT results in a marked reduction in vessel permeability that extends beyond the macular area itself (see *Figure 1*).

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Our experience refers to 13 patients (15 eyes) treated between 2004 and 2006 for macular oedema secondary to CNU in non-vitrectomised eyes. Macular thickness reduction on ocular computerised tomography (OCT) scans was significant in all eyes. VA improved in 11 eyes (87%) and remained unaltered in two eyes (13%). We speculate that those eyes in which there was no VA improvement had suffered irreversible photoreceptor damage due to long-standing oedema. Thus, time is an important factor to consider when treating these patients and, generally, all patients with macular oedema. Another important issue that is applicable to CNU cases – as well as to others, as discussed below – is the necessity to re-treat with IVT. In this series, only six of the eyes (55%) that had shown improvement in VA remained stable at six months, whereas in the remaining five eyes (45%) VA deteriorated over three to six months, necessitating re-treatment with IVT. Two eyes (one patient) in this group were lost to follow-up.

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A further issue to be addressed in CNU patients is the timing of vitrectomy, when necessary, in relation to IVT. Whenever residual vitreous opacities hinder visual function, vitrectomy is appropriate. We always perform full vitrectomy with posterior hyaloid removal and internal limiting membrane (ILM) peeling. Regardless of whether an OCT scan is obtainable, we always assume macular oedema to be present. Given that IVT is less effective in vitrectomised eyes, we generally introduce IVT at least three weeks before the vitrectomy is performed. A further benefit of this approach is that the reduced macular thickness will result in a reduced risk of damaging the macula while peeling the ILM. There are obviously exceptions to this approach, mainly in cases where a tractional retinal detachment is detected and vitrectomy cannot be postponed. The application of these general concepts is therefore at the surgeon's discretion. Much has been written on this topic.[5,6] A detailed discussion of the different forms of clinical presentation and natural history of the condition is beyond the scope of this paper; however, a retrospective study on 125 patients who we treated between 2004 and 2007 allows us to draw the following conclusions, which are, overall, in line with most authors' reports:

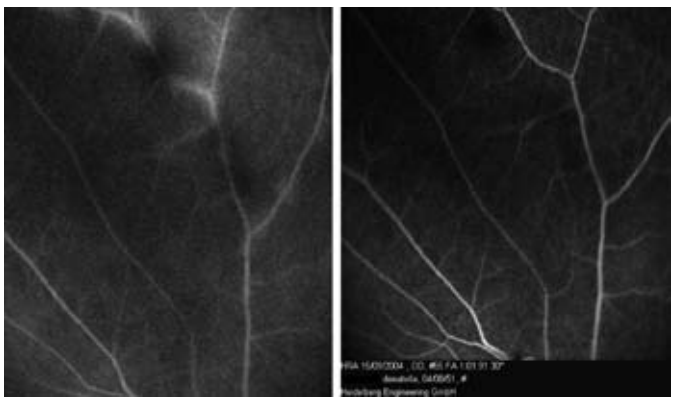
- IVT is effective in treating diabetic macular oedema. Recent data[7] seem to indicate that diabetic cystoid macular oedema

Table 1: Comparison of Triamcinolone and Other Steroids

Glucocorticoid Preparations – Estimated Potency*		
Commonly Used Name**	Glucorticoid	Mineral Corticoid
Short-acting		
Cortisol	1	1
Cortisone	0.8	0.8
Intermediate-acting		
Prednisone	4	0.25
Prednisolone	4	0.25
Methylprednisolone	5	<0.01
Triamcinolone	5	<0.01
Long-acting		
Paramethasone	10	<0.01
Betamethasone	25	<0.01
Dexamethasone	30-40	<0.01

** Relative milligram comparisons with cortisol, setting the glucocorticoid and mineral corticoid properties of cortisol as 1.*
*** The steroids are divided into three groups according to the duration and biologic activity. Short-acting preparations have a biologic half-life of less than 12 hours; long-acting greater than 48; and intermediate between 12 and 36. Triamcinolone has the longest half-life of the intermediate group.*

Figure 1: Periphlebitis and Associated Vascular Leakage Is Reduced Three Weeks After Intravitreal Triamcinolone Acetonide Has Been Administered



(CMO) responds better to treatment than diffuse diabetic macular oedema (DDMO).

- A reduction in macular thickness does not necessarily correlate with a gain in VA. Time elapsed from the onset of the condition, its severity, the amount of ischaemia present and the formation of hard exudates all play a role in the degree of visual rehabilitation that can be achieved.
- Even DDMO associated with a microtractional component responds to IVT. This treatment alone may result in a satisfactory improvement in VA, or may represent a stepping-stone to vitrectomy with a reduced risk of macular damage.
- Theoretically, reduced vessel permeability should result in reduced formation of hard exudates.[8] However, in reality this may not always be the case (see *Figure 2*). We generally treat patients with hard exudates by focal laser photocoagulation, taking advantage of the reduced retinal thickness obtained with IVT, which allows the use of lower power settings.
- It should be kept in mind that good metabolic control is essential for preventing and limiting retinal complications. The ophthalmologist's role is to reduce the impact of such complications and to 'buy time' until the patient has attained more satisfactory control of blood sugar levels. Thus, repeated IVT treatment may be necessary to maintain useful vision.
- We have found, in agreement with other authors,[9] that IVT compares favourably with macular grid laser photocoagulation (MGLP). In those patients in whom stable results cannot be obtained with repeated IVT injections and no tractional component is present on OCT, IVT+MGLP may represent the only possible option.

As the newer anti-VEGF drugs gain popularity, it remains to be seen what future role IVT will play in the treatment of diabetic macular oedema.

Pseudophakic Macular Oedema

Although not all of the mechanisms involved in this pathology are clearly understood, there is a general agreement that it is a multifactorial event that involves both an inflammatory response and a vascular component. Not all authors agree on the efficacy of IVT in the treatment of this particular kind of oedema.[10] In a retrospective case series of 47 patients with an excellent response to IVT – characterised by rapid improvement in VA and relatively stable results (see *Figure 3*) – we found that 13 (27%) suffered a relapse of the condition and needed further IVT injections.

Other Forms of Macular Oedema

Other forms of macular oedema may also benefit from the use of IVT. Branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) have a visual prognosis that depends on many factors, including the extent of the area affected, its proximity to the macula (BRVO), the amount of ischaemia present and the age and general vascular status of the patient. Much of the damage that occurs, especially in cases that would seem to hold a relatively good prognosis, derives from the macular oedema that invariably develops and that generally persists before any laser treatment can be attempted.

IVT is efficacious in reducing macular oedema,[11,12] thus buying time until either sufficient artero-venous shunts develop to allow proper drainage of the affected area or focal laser treatment can be applied. Reports[13] on the use of combined IVT and anti-VEGF therapy for cases of CRVO refractory to single-drug treatment warrant further investigation. We have had successful results in treating cases of macular oedema related to acute systemic hypertension retinopathy and radiation retinopathy with IVT and focal laser treatment.

Choroidal neo-vascularisation (CNV) is another field in which IVT has been used. Selected cases treated with photodynamic therapy (PDT) seem to benefit from the use of IVT because of the reduction in macular oedema induced by the drug. In addition, there may be anti-VEGF action that enhances treatment of PDT.

Triamcinolone as a Surgical Tool

Triamcinolone acetonide is available in a suspension form. The dispersed crystals adhere to the collagen fibrils, thus making vitreous identification easier. We use the drug intra-operatively as an aid to identifying and removing the posterior hyaloid. Caution should be used when macular hole surgery is performed, as the crystals have a tendency to migrate into the hole itself, as well as underneath the retina. Although there is as yet no evidence to confirm this, the triamcinolone granules could somehow interfere with VA recovery.

Complications and Side Effects

All intravitreal injections, including of triamcinolone, must be

Figure 2: Intravitreal Triamcinolone Acetonide Treatment in this Diabetic Patient Resolved the Macular Oedema that Was Present, but Did Not Prevent a Hard Exudate From Forming

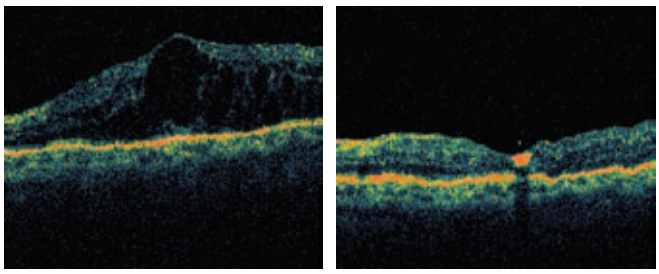
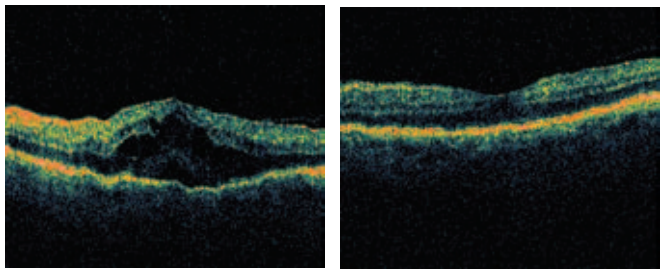


Figure 3: Rapid Improvement (two weeks) of Pseudophakic Macular Oedema Following Intravitreal Triamcinolone Acetonide



performed under sterile conditions with the same approach one would use for other intraocular procedures. The drug must be filtered before it is used, thus preventing the solvent from being introduced to the eye. Many of the so-called pseudo-endophthalmitis (sterile endophthalmitis) cases reported in the past were attributable to the inflammatory reaction induced by the solvent before filtration was adopted for the procedure. True endophthalmitis has a much worse prognosis in these eyes compared with eyes in which endophthalmitis develops after cataract surgery. The reasons for this are obvious, since the infective agent develops directly within the vitreous in proximity to the retina rather than in the anterior chamber. Therefore, we recommend that follow-up visits be tightly scheduled in the first 48 hours following the procedure, ideally with the first consultation taking place in the first eight to 12 hours. Vitreous incarceration at the site of injection should be avoided. We recommend an anterior chamber paracentesis immediately before IVT is performed.

> The main side effect of intravitreal triamcinolone acetonide is ocular hypertension, which can generally be effectively controlled.

The data related to ocular hypertension resulting from IVT treatment vary according to different authors. Of the 146 eyes we treated with IVT for macular oedema of various aetiologies, 47 (32%) developed clinically significant intraocular hypertension. The spike in intraocular pressure (IOP) occurred six to 10 weeks after IVT treatment. Control of IOP was achieved in all patients either with topical medication alone (37 eyes) or with the adjunct of argon laser trabeculoplasty (ALT) (10 eyes). In our experience, ALT seems to work dramatically well in this form of hyatrogenic ocular hypertension. None of our patients required glaucoma surgery. There are no specific data on the incidence of cataract exclusively related to IVT.

Conclusions

IVT is effective in treating macular oedema secondary to a variety of ocular conditions. Its efficacy in restoring VA is not only related to the specific pathology, but is probably also dependent on the time elapsed between the onset of the oedema and its treatment.

Complications associated with the use of IVT are similar to those found in any other procedure involving penetration of the vitreous cavity (i.e. anti-VEGF injections). The main side effect of the treatment is ocular hypertension, which can generally be effectively controlled. The major limitation of the treatment, in our view, is the need to re-treat many of these patients for relapses of macular oedema and associated deterioration in VA. Although the industry is about to introduce a specific product, at present triamcinolone acetonide is not intended for ophthalmic employment. This 'off-label' use of the drug implies that special attention must be taken in obtaining fully informed consent from the patient. ■

Acknowledgements

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