INTRAVITREAL STEROIDS IN RETINAL DISEASES-A BOON

Dr. Ajay Dudani, Dr. Reshma Jhaveri

effects, although the mode of action of triamcinolone on human choroidal endothelial cells remains to be completely defined.

INDICATIONS:

1) Treatment of diabetic retinopathy,

2)Cystoid macular oedema (CMO) associated with uveitis, or Irvine Gass Syndrome

3)Birdshot retinochoroidopathy.

4)Exudative age related macular degeneration (AMD).

5)Central retinal and Branch retinal vein occlusion

6)Neovascular Glaucoma[6]

7)Ischaemic ophthalmopathy

8)Choroidal neovascularisation in ocular histoplasmosis.[4]

9)Radiation induced macular odema[5]

10)Exudative retinopathies

11)Eales Disease

12)Bilateral acquired parafoveal talangiectasis

Dosage: 2-4mg\0.1ml

The ISIS (Intravitreal Steroid Injection Studies): is a nine-center, dose-controlled pilot study .This study will evaluate the safety and effectiveness of a new formulation of triamcinolone acetonide for the treatment of retinal blood vessel disorders. Triamcinolone is a steroid drug that decreases inflammation and scarring and is routinely used to treat eye inflammation or swelling. The commercially available form of this drug is associated with potentially harmful side effects thought to be due to preservatives in the preparation. This study will use a formulation that does not contain these potentially harmful preservatives. Preliminary findings from other studies suggest that injection of steroids in the eye can reduce retinal thickening and improve vision. However, they may also cause mild discomfort and lead to vision-threatening conditions. The effects of the drug on the conditions under study in this protocol are not known.

INTRODUCTION:

Steroids are potent anti-inflammatory agents. They are thought to inhibit production of vascular endothelial growth factor(VEGF) and have been shown to decrease the breakdown of the blood-retinal barrier.[1,2] These qualities make steroids a potential treatment in many retinal disorders. Steroids have been a mainstay of treatment for ophthalmic diseases for decades.

The various modes of administration of steroids include :

1) Systemic administration: It carries the great risk of side effects, some of which are quite serious. 2) Topical administration of steroid: It is the easiest and has the least risk of side effects, this route of administration is also probably least effective due to limited drug delivery to the retina.3) Retrobulbar or subTenon's injections have for many years offered a compromise between better penetration and avoidance of systemic side effects.4) Intraocular administration of drugs has typically been reserved for vision-threatening conditions such as endopthalmitis. The perceived risk/ benefit ratio of intraocular injections for the other indications has been influenced by concerns of introducing an infection, detaching the retina, or drug toxicity. In the past years, the use of intraocular injections of steroids for a variety of conditions is being explored by investigators.

Intravitreal dexamethasone has been very often used for treatment of endophthalmitis. Multiple studies are been carried out to employ intravitreal triamcinolone acetonide (IVTA) in the treatment of various retinal disorders.

Mode of Action:

Triamcinolone has the capacity to modulate *epithelial* cell resistance . The findings are consistentwith clinical observations indicating that reduction of the permeability of the outer blood-retinal barrier, resorption of exudation, and downregulation of inflammatory stimuli are the principal effects of intravitreal triamcinolone.[3] Glucocorticoids are known to display differential capacities to mediate antiangiogenic, anti-inflammatory and permeability

II) Of the Therapy:

a) Raised intraocular pressure

b) Cataract formation

c) Rarely endophthalmitis

EFFICACY OF INTRAVITREAL STEROIDS Over the past year there has been a great deal of excitement about the possibility of utilizing a common steroid, Kenalog, in a unique fashion, intravitreal injection, to treat retinal diseases. Intravitreal steroid injections have been proven to be safe (approximately 0.2% incidence of infection) and effective in treating retinal swelling. The immediate impact of intravitreal kenalog on retinal swelling and vision can be dramatic. Intravitreal steroids use for diffuse diabetic retinal edema, retinal edema associated with retinal vein occlusions and chronic post operative macular edema has been effective. The indications for intravitreal steroid injections are still evolving. In most cases, angiographic retinal edema improves about 2 weeks following injection. Vision recovery tends to occur 1-2 months later. Repeat injections may be necessary to achieve the desired results given the possibility for recurrent leakage after many months following the injection. Intravitreal steroids are powerful and very helpful in treating difficult retinal diseases which have not responded to laser and topical steroid drops. The use of intravitreal steroids has become a standard of care in contemporary retina practices.

LIFE SPAN OF THE DRUG: In Diabetics it usually works consistently for four to five months after which a reinjection is required in about 35 % of cases. In CVO or CME post cataract it typically works for about three months where there may be a visual improvement of three lines.

POINTS TO PONDER

Many questions regarding the use of intravitreal steroids remain unanswered.

1) Whether it will give a sustained improvement.

2) How long would the effect of the injection last.

3) If it can be used as a primary treatment or only as an adjunct to other modalities.

4) What is the appropriate dosage of the drug for a given retinal disorder.

Patients with the following conditions involving disorders of retinal blood vessels may be eligible for this study:1)- Choroidal neovascularization associated with age-related macular degeneration (50 years of age and older) 2)- Macular edema associated with retinal vein occlusion (18 years of age and older) 3)- Diabetic macular edema ((18 years of age and older)

Route of Administration: 1) Direct intravitreal administration: The medication is injected through the pars plana under topical anesthesia, in strict aseptic conditions, usually in the inferior quadrants to avoid dispersion of the suspension over the central vision. Direct injection of triamcinolone acetonide also shows promise for the treatment of diabetic macular edema.[7]

2) Systems intravitreal implant of fluocinolone acetonide for treatment of macular edema (FAME 4 Study). This implant is a steroid compound pellet incorporated into a plastic strut. The implant is placed through the pars plana and the strut is secured to the sclera with suture. It does not interfere with vision, since the implant is placed far into the periphery and does not extend into the visual axis. It is similar in appearance and function to the ganciclovir intravitreal implant (used for cytomegalovirus retinitis, allowing a slow release of medication over a prolonged duration. The fluocinolone is released over three years, supplying a constant flow of medication to the retinal vessels.

3) Another clinical trial is evaluating Oculex Pharmaceuticals' dexamethasone posterior segment drug delivery system (DEX PS DDS). The study is a Phase II trial of the steroid implant in the treatment of persistent macular edema. The dexamethasone is incorporated in a biodegradable polymer platform designed for the slow release of the steroid over approximately four to five weeks, with complete bioresorption of the polymer platform over 50 to 160 days. It is inserted through the pars plana and is smaller than a pencil tip. The pellet lodges in the vitreous base, delivering medication to the posterior segment.

COMPLICATIONS:

I) Of the procedure:

A) Infection

B) Retinal detachment

c) Hemorrhage

4Amj Ophthalmology 2003 136(4)

5.Arch ophthalmology2003 oct121(10)1491-3

6.Acta Ophthalmol Scnd 2003oct 81(5)540-1 7 Martidis A, Duker JS, Greenberg PB, Rogers AH, Puliafito CA, Reichel E, Baumal C. Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology 2002;109:920-927.

Contact Details

Zen Eye Center
Tel. : 26047104

5) What is the safety of the drug.

References:

1. Martidis A, Duker JS, Greenberg PB, Rogers AH, Puliafito CA, Reichel E, Baumal C. Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology 2002;109:920-927.

2. Wilson CA, Berkowitz BA, Sato Y, Ando N, Handa JT, de Juan E Jr. Treatment with intravitreal steroid reduces blood-retinal barrier breakdown due to retinal photocoagulation. Arch Ophthalmol 1992;110:1155-1159.

3. Penfold PL, Wong JG, Gyory J, *et al*. Effects of triamcinolone acetonide on micoglial morphology and quantitative expression of MHC-II in exudative AMD. *Clin Exp Ophthalmol* 2001;29:188–92.