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MAJOR REVIEW

Intraocular Pressure Monitoring Post Intravitreal Steroids: A Systematic Review

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Abstract. The use of intravitreal (IVT) corticosteroids for treatment of posterior segment diseases has increased significantly over the last decade. A commonly recognized complication of IVT steroids is secondary ocular hypertension (OHT) that can occur immediately secondary to direct intraocular volume increase or weeks to months later as a result of increased outflow resistance. We performed a meta-analysis and found 32% (95% confidence interval, 28.2–36.3) of individuals developed OHT following 4 mg IVT triamcinolone, 66% (50.2–78.8) and 79% (72.2–84.5) following 0.59 and 2.1 mg fluocinolone implant, respectively, and 11% (6.4–17.9) and 15% (9.2–24.3) following 0.35 and 0.7 mg dexamethasone implant, respectively. Risk factors included pre-existing glaucoma, higher baseline intraocular pressure (IOP), younger age, OHT following previous injection, uveitis, higher steroid dosage, and fluocinolone implant. Most cases of OHT can be controlled medically; up to 45% following fluocinolone implant require surgery, however. We suggest a protocol to monitor IOP after IVT steroid injection/implantation that includes checking IOP within 30 minutes after injection, followed by 1 week after IVT triamcinolone and 2 weeks after implant insertion, then every 2 weeks for the first month and monthly for up to 6 months after IVT triamcinolone and dexamethasone implantation and 9 months after fluocinolone implantation. (**Surv Ophthalmol 58**:291–310, 2013.

Key words. ocular hypertension • steroid-induced glaucoma • intravitreal steroid injection • sustained-release intravitreal implants

I. Introduction

A. STEROIDS AND INTRAOCULAR PRESSURE

Exogenous steroids administered topically (by peri- and/or intraocular injection) or orally can cause secondary ocular hypertension (OHT).[5,197] The risk of inhaled nasal sprays causing secondary OHT is less clearly defined.[200] The risk of steroid-induced OHT varies by route of administration, duration of treatment, type of steroid, and pre-existing history of glaucoma, among other factors. For example, approximately 40% of the general population developed OHT after a 4–6 week course of topical 0.1% dexamethasone, so-called steroid responders, compared with nearly 100% of patients

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with primary open-angle glaucoma (POAG) or normal-tension glaucoma.[3,4,138]

The etiology of steroid-induced OHT has been linked to the myocilin gene that is upregulated by steroid treatment in cultured trabecular meshwork cells.[158] Stone et al reported that myocilin gene mutations were also associated with development of POAG.[180] Although steroid-induced OHT usually reverses after cessation of steroid administration, it remains an important risk factor for the development of glaucomatous optic neuropathy.[3,196] A protocol for intraocular pressure (IOP) monitoring following steroid administration is essential to limit visual function loss secondary to steroid-induced glaucoma.

B. INTRAVITREAL STEROIDS

The use of intravitreal (IVT) corticosteroids has increased significantly over the past 10 years because of their beneficial effects on macular edema secondary to uveitis, venous occlusive disease, diabetes, and choroidal neovascularization.[13,26,44,74,90,98,120,184,189] The two main methods of IVT steroid delivery are injection and implantation of sustained-release devices. Despite the knowledge that IVT steroids may cause significant elevations of IOP, with 1–8% and up to 45% of patients reportedly requiring surgery for uncontrolled IOP after IVT triamcinolone acetonide (TA) injection and fluocinolone acetonide (FA) implantation, respectively, there is no consensus regarding the monitoring of IOP.[23,156,191] There are a few published reviews on IOP elevation following IVT steroids; we found no systematic literature review or meta-analysis of this important topic, however.[97,108,191]

We provide the results of a systematic literature review and meta-analysis. Our objectives are to describe the frequency, onset, duration, magnitude, management, and risk factors of IOP elevation following IVT steroids and to develop a best-practice recommendation for IOP surveillance following IVT steroid administration.

II. Intravitreal Steroid Delivery Methods

A. INTRAVITREAL INJECTION

The injection of steroid directly into the vitreous allows a large bolus of drug to be administered to achieve a desired therapeutic level at the target tissue while minimizing systemic absorption and side effects. The most common steroids used for an IVT injection are TA and dexamethasone.

1. Triamcinolone Acetonide Intravitreal Injection

TA (Kenalog, Bristol-Myers Squibb, New York, NY) is a crystalline steroid that is minimally water soluble injected in a suspension form. IVT TA had been studied in different doses: 1, 2, 4, 5, 6, 8, 10, 20, and 25 mg.[48,95–97,101–103,106,107,133,164] In most studies, a dose of 4 mg is used. The therapeutic response and duration of action can last approximately 3 months following 4 mg IVT TA.[20]

2. Dexamethasone Intravitreal Injection

Dexamethasone (dexamethasone sodium phosphate, Weimer Pharma GmbH, Rastatt, Germany) is more potent with a shorter duration of action compared with TA.[199] When given intravitreally it has been shown to be safe in dosages up to 1 mg.[72] IVT dexamethasone had been studied in two doses: 0.4 and 0.8 mg.[33] Although the short duration of action of dexamethasone may minimize side effects it also may limit its therapeutic effect. A single injection of IVT dexamethasone did not have a beneficial effect on diabetic macular edema (DME).[33] There are few studies reporting IVT dexamethasone for treatment of posterior segment diseases.

B. SUSTAINED-RELEASE INTRAVITREAL IMPLANT (FIG. 1)

Given the short half-life of IVT steroids, repeated injections may be required to maintain therapeutic effects, increasing the risk of injection-related complications such as retinal detachment, vitreous hemorrhage, and endophthalmitis.[20,72] This has led to the development of sustained-release implants.[60] IVT implants are classified as either non-biodegradable or biodegradable. Non-biodegradable implants provide more accurate drug release and longer duration of action than the biodegradable implants, but require surgical removal.[25,187]

1. Triamcinolone Acetonide Sustained-Release Implant

I-vation (SurModics, Eden Prairie, MN) (Fig. 1A) is a helical-shaped non-biodegradable metallic implant designed to deliver TA for 24 months. Phase II trials of I-vation for DME were suspended by Merck because photocoagulation was more effective than IVT TA as a treatment for DME.[19,57]

2. Fluocinolone Acetonide Sustained-release Implant

a. Retisert

Retisert (Bausch and Lomb, Rochester, NY) (Fig. 1B) is a non-biodegradable IVT FA implant that is inserted via the pars plana. The device is sutured to the sclera and releases FA at a controlled rate for approximately 30 months. Retisert had been