Intraocular Pressure Changes after Triamcinolone Acetonide Intravitreal Injection

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Abstract

Aim: To investigate the intraocular pressure (IOP) response after intravitreal triamcinolone acetonide (IVTA) injections as treatment of intraocular neovascular or oedematous diseases and the ability to predict secondary steroid-induced glaucoma.

Methods: The prospective consecutive comparative interventional case series study included 80 eyes of 76 patients, group (A), 40 eyes; group (B), 40 eyes, who received an intravitreal injection of 4mg triamcinolone acetonide and had a follow-up time of 1 weeks interval for 6 weeks. In group (B), topical prednisolone acetate (0.1%) was administrated 3 times daily for 2 weeks before injection, and the follow-up started 1 day before injection.

Results: In group (A) IOP increased significantly ($p=0.001$) from 13.8 (1.9) mmHg preoperatively to a mean maximum of 15.6 (2.7) mmHg postoperatively. An IOP rise to values higher than 20mmHg was observed in 6 (15%) eyes. Elevation of IOP occurred 1 week after the injection. In group (B) IOP increased non significantly ($p>0.001$) from 14.8 (2.1) mmHg preoperatively to a mean maximum of 16.35 (2.7) mmHg (range 13-24mmHg) postoperatively. 5 (12.5%) of patients in group B showed significant elevation of IOP (>25mmHg) after topical administration of prednisolone acetate and were excluded from injection. 4 of them were managed by topical B-blockers, and 1 eye required trabeculoplasty. Preoperative predictive factor for the rise in IOP was younger age ($p=0.0002$). It was statistically independent of refractive error, presence of diabetes mellitus, and indication for the injection. In all but two eye, IOP could be lowered to the normal range with topical medication during the follow-up period, without development of glaucoma tosaic nerve head changes.

Conclusions: After intravitreal injections of 4mg of triamcinolone acetonide, an IOP elevation can develop in about 25% of eyes starting 1 week after injection, but the onset is inconstant in all cases. In the vast majority, IOP can be normalized by topical medication. Topical steroid administration pre-injection helped knowing the steroid responders and non-responders, so avoiding the occurrence of 2 ry refractory glaucoma steroid-injection.

Key Words: Glaucoma – Diabetic macular – Intraocular injection – Triamcinolone acetonide.

Fluorescein angiography and optical coherence tomography (OCT) before (A), and OCT 6 weeks after intravitreal injection of triamcinolone acetonide (B). Note: Central corneal thickness before (557 µ) and after (325 µ).
Introduction

INJECTION Intravitreal triamcinolone acetonide has increasingly been used in previous studies as treatment for intraocular proliferative, edematous, and neovascular diseases, such as central retinal vein occlusion, neovascular glaucoma without or with cataract surgery, chronic pre-phthisical ocular hypotony, chronic uveitis, persistent pseudophakic cystoid macular edema, exudative age-related macular degeneration, proliferative diabetic retinopathy, ischemic ophthalmopathy, sympathetic ophthalmia, and in other clinical situations \[1\]. Direct intraocular injection of steroids delivers the desired drug to its target tissue in the most direct fashion without extraocular side effects as that happened after oral steroids administration. After a single intravitreal injection of triamcinolone acetonide, one can deliver a concentration of thousands of nanograms of triamcinolone to the vitreous cavity. Drug concentrations rapidly decrease and are followed by a subsequent prolonged rate of elimination. A measurable concentration is maintained in the vitreous humor for approximately 90 days \[2\].

Side effects reported so far include cataract; secondary ocular hypertension leading in some patients to secondary chronic open-angle glaucoma; and post injection, infectious, or sterile endophthalmitis \[1\]. Previous studies have shown that one of the most common side effects of intravitreal triamcinolone acetonide was a steroid-induced elevation of IOP \[3\]. Since previous studies examined the rate and amount of elevation of IOP after topical application of cortisone leading to much lower intraocular concentrations of steroids than if the steroids were injected intravitreally, we aimed to evaluate the response of IOP after the intravitreal injection of corticosteroids. As well as the IOP changes when the intravitreal triamcinolone acetonide injection is preceded by administration of topical steroid as a provocative test.

Patients and Methods

Patients were selected outpatient Cairo and Beni-Swif Universities from 2010-2011.

The prospective interventional case series study included 76 patients (80 eyes) divided into 2 groups. Group A included 36 patients (40 eyes) (22 women, 18 men; 16 right eyes, 24 left eyes) who consecutively received an intravitreal injection of 4mg triamcinolone acetonide with topical anaesthesia, and who had a follow-up time of 6 weeks. Group B included 40 patients (40 eyes) (24 women, 16 men; 22 right eyes, 18 left eyes) who consecutively received topical prednisolone acetate (0.1%) 3 times daily for 2 weeks as a provocative test prior to triamcinolone acetonide intravitreal injection. The reason for the intravitreal injection of triamcinolone acetonide were progressive decrease of visual acuity due to exudative agerelated macular degeneration with subfoveal neovascularization (n=11 eyes), or diffuse diabetic macular oedema (n=68 eyes) or Retinal vein occlusion (1 eye). Mean age was 50.4 (9.5) years (range 20.1-65.1 years). All patients were fully informed about the experimental character of the therapy. All patients signed an informed consent. The ethics committee of the university had approved the study.

Fluorescein angiography and optical coherence tomography before (A-C), and 6 weeks after (B-D) intravitreal injection of triamcinolone acetonide. Note: Decrease in fluorescein leakage and decrease in retinal thickening.
Patients received an intravitreal injection of 4mg of crystalline triamcinolone acetonide under sterile conditions in the operating theatre. The solution was prepared by the hospital’s pharmacy removing the solvent agent. Using the operation microscope, the injection was transconjunctivally carried out under topical anaesthesia after a para-centesis had been performed to decrease the volume of the globe. Using applanation tonometry, IOP was determined before, and in intervals of 1 week after the injection for 1 month.

For inter individual comparisons, only one randomly selected eye per patient was taken for statistical analysis. For intra individual bilateral comparison, the four patients with both eyes treated were included in the analysis.

**Results**

In group A, IOP increased significantly ($p<0.001$) from a mean initial pressure 13.8 (1.9) mmHg (range 10-17mmHg) to a mean maximum of 23.38 (8.37) mmHg (range 13-64mmHg) post-operatively. The differences between the IOP measurements before the injection and the postoperative examinations were significant ($p<0.05$). For the examinations performed 1 week or later after the injection, a rise in IOP to values higher than 21mmHg was observed in 6 (25%) eyes. The elevation of IOP usually occurred within the first week.

The post-injection rise of IOP to values higher than 21mmHg was statistically independent of refractive error ($p=0.35$), sex ($p=0.1078$). In group B, 5 eyes (12.5%) showed significant transient increase in IOP after topical prednisolone acetate administration and were excluded from the intravitreal triamcinolone acetonide injection, 4 of them returned to the normal levels using only topical B-blockers, and only 1 eye turned into refractory glaucoma and required trabeculoplasty as a treatment. The rest of the group B showed a mean initial pressure 14.8 (2.1) mmHg (range 12-18mmHg) to a mean maximum of 16.8 (4.9) mmHg (range 10-34mmHg) post-operatively. A rise in IOP to values higher than 21mmHg was observed in 4 (10%) eyes after intravitreal injection. Young age showed more liability to develop high IOP following intravitreal injection of TA it was statistically significant ($p=0.0002$).

**Discussion**

Intraocular neovascular diseases, such as exudative age related macular degeneration and proliferative diabetic retinopathy, oedematous diseases of the retina, such as diffuse diabetic macular oedema and persistent cystoid macular oedema due to various other diseases, and chronic intraocular inflammation are some of the leading causes of impaired vision. The intraocular proliferation of cells is often accompanied and stimulated by intraocular inflammation, and macular oedema can be caused by a damaged blood-retinal barrier due to capillary leakage. Corticosteroids have long been known to tighten up blood vessels resulting in a decrease of vessel leakage and, depending on the concentration, to suppress proliferation of cells. Consequently, steroids have been used for the treatment of various ocular diseases, applied either topically or systemically. Often, however, the intraocular concentrations of corticosteroids were not sufficiently high, or the systemic side effects were too serious, to effectively treat the ocular disorder.

Taking into account that the eye comprises only 0.01% of the entire body volume, and considering that for achieving a high concentration of a drug at its site of action, it is best to apply it directly in the area of required action, Machemer, Graham, Peyman, and other researchers studied the possibility of injecting corticosteroids directly into the eye, in experimental settings in animals as well as in selected clinical situations in patients [4-6]. Additionally, observations of clinical outcome after accidental intraocular injections of cortisone have been published [4,8]. In experimental investigations, Machemer and coworkers had observed that the vehicle, and not the crystalline corticosteroid itself, can be toxic to intraocular tissues [9,10]. Correspondingly, a direct toxicity of high intraocular concentrations of corticosteroids has not been detected in ongoing studies so far. The presented studies demonstrated that a single intraocular injection of triamcinolone acetonide may potentially be helpful as adjunctive treatment of proliferate diabetic retinopathy, clinically significant diabetic macular oedema, neovascular glaucoma, and phthysiological ocular hypotony [11-28]. In the latter studies, as suggested by Machemer, a crystalline corticosteroid (triamcinolone acetonide) was taken which remains in the eye for 2-5 months after a single intravitreal injection, in contrast with a soluble corticosteroid which is washed out of the eye within 24 hours after intraocular application [32]. One of the major side effects, which are most often discussed in combination with an intravitreal injection of triamcinolone acetonide, is a steroid induced elevation of IOP [29-31]. The results of the present study showed that a rise of IOP to values higher than 21mmHg can be expected to occur in
about 25% of the eyes treated. A predictive factor for the rise of IOP may have been the presence of glaucoma before the injection. This relation, however, was statistically not significant.

But a statistically significant relation was found for the younger age with a post-injection rise in IOP. Other parameters, such as sex and refractive error of the patient did not show a marked influence on frequency and amount of the elevation of IOP. Interestingly, the presence of diabetes mellitus did not demonstrate a marked influence on the rate of a postoperative elevation of IOP. From a clinical point of view it may be important that in all but one eye, the IOP could be controlled by topical antiglaucomatous treatment. Also, as to be expected, both eyes of the same patient reacted in a similar way, if both eyes received an intravitreal injection.

In contrast with other clinical studies reporting on the intravitreal injection of triamcinolone acetonide, the dosage used in the present investigation was about five times higher (20mg versus 4mg) [12-16,18,19,24,25,27,28,33-35,36]. Without starting a discussion on the clinical usefulness and necessity to use a remarkably higher dosage than in other studies, the results of the present investigation demonstrate that also with this high dosage of intravitreal triamcinolone acetonide, the steroid induced elevation in IOP can also be controlled without development of a major damage to the optic nerve.

In conclusion, the data of the present study suggest that the intravitreal injection of triamcinolone acetonide in a dosage of 20mg leads to a secondary ocular hypertension in about 25% of the eyes treated; that the rise of IOP can usually be controlled by topical antiglaucomatous medication. Topical steroid administration pre-injection helped knowing steroid responders and non-responders, so avoiding the occurrence of 2 ry refractory glaucoma.

References


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