ORIGINAL ARTICLE

Frequency and Management of Raised Intraocular Pressure Following Intravitreal Triamcinolone Acetonide

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ABSTRACT

Objective: To determine the frequency and management of intraocular pressure (IOP) elevation following intravitreal triamcinolone acetonide (IVTA).

Study Design: Case series.

Place and Duration of Study: Isra Postgraduate Institute of Ophthalmology/Al-Ibrahim Eye Hospital, Karachi, from May 2007 to May 2008.

Methodology: In this study, 198 eyes of 150 patients requiring IVTA injection, were included. Pre-injection assessment comprised of detailed history, general and ocular examination including anterior and posterior segment examination with IOP measurements with Goldmann tonometer. After informed consent, IVTA 4 mg/0.1 ml was injected through pars plana and IOP was measured at 1 week, 1 month, 3 months and 6 months and if raised, treated accordingly.

Results: Out of 150 patients, 82 were male (54.7%) and 68 were female (45.3%) (M: F = 1.2: 1). Mean age was 50.61 ± 10.59 years. Raised IOP value after IVTA, higher than 21 mmHg was observed at one week in 28 eyes (14.1%), at 1 month in 48 eyes (24.2%), at 3 months in 76 eyes (38.4%) and at 6 months in 25 eyes (12.6%). Raised IOP was controlled by topical beta blockers alone or in combination with carbonic anhydrase inhibitors in 58 eyes (76.3%).

Conclusion: Elevation of IOP after IVTA injection occurred in 76 eyes (38.3%). It may take an extended period of time to manifest raised IOP. In majority of the patients, raised IOP was managed with topical medications.

Key words: *Glaucoma. Corticosteroids. Intraocular pressure. Intravitreal steroid. Topical beta blocker.*

INTRODUCTION

Triamcinolone acetonide is one of the synthetic glucocorticoids used for its anti-inflammatory effect in disorders of many organ systems. Intravitreal triamcinolone acetonide (IVTA) is being used to treat a variety of ocular diseases such as cystoid macular oedema after cataract surgery, macular oedema due to inflammatory conditions e.g. uveitis,[1] birdshort retinochoroidopathy, retinal vascular diseases e.g. branch retinal vein occlusion (BRVO),[2] central retinal vein occlusion (CRVO),[3] diabetic maculopathy,[4] neovascular age-related macular degeneration (ARMD) and diabetic papillopathy.

Although the exact mechanism of the action of corticosteroid induced reduction of macular oedema is yet to be known, there have been several proposed hypothesis, including a local reduction of inflammatory mediators, increased diffusion by modulation of calcium channels, tightening of endothelial cell junctions, reduction of capillary permeability and decreased level of the vascular endothelial growth factor, resulting in stabilization of blood retinal barrier. However, the treatment is not without its risks.

Reported complications of IVTA include raised intraocular pressure (IOP).[5] The exact mechanism for raised IOP is not known. It is an open angle type of glaucoma, more common in steroid responders. It may be caused by cortisone crystals blocking trabecular meshwork or by decreased phagocytosis of extracellular matrix in the trabecular meshwork by macrophages. Other reported complications of IVTA include posterior sub-capsular lens opacities and non-infectious endophthalmitis.[6]

The most common complication after IVTA is a transient increase in IOP.[5] It is reported that baseline IOP greater than 16 mmHg is a risk factor for post-injection IOP elevation.[7] The IOP elevation may take extended period of time to manifest and may rarely require filtration surgery.

The objective of this study was to assess the frequency of raised IOP after IVTA and its management.

METHODOLOGY

This prospective, interventional case series was conducted at Isra Postgraduate Institute of Ophthalmology, Al-Ibrahim Eye Hospital, Karachi, from May 2007 to May 2008. The permission of the study was granted by the hospital's ethical committee. Consecutive patients requiring IVTA injection for any of the approved indications were inducted. Patients having IOP of more

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than 20 mmHg, already receiving anti-glaucoma medicines were excluded from the study.

After informed consent, a detailed ophthalmic examination was carried out to include best corrected visual acuity (BCVA), anterior segment slit lamp biomicroscopy, IOP measurement with Goldmannn applanation tonometer and Goldmann double mirror gonioscopy. A dilated fundus examination was performed using +90DS lens for the diagnosis of retinal pathology. All data regarding patient's examination, diagnosis, treatment and follow-up were entered in a pre-designed proforma.

One day prior to injection, patients were commenced on ciprofloxacin drops 0.3% (Ciloxan - Alcon, Belgium) 4 times a day. Next day patients were taken to the operating room, where after applying povidone-iodine 5% for 5 minutes, triamcinolone acetonide 4 mg/0.1 ml was injected in the vitreous cavity 3.5 mm away from the limbus under the influence of topical anaesthesia using operating microscope.

Patient's anterior segment was examined with measurement of IOP, 2 hours after the procedure and topical antibiotic drops were continued for next 3 days. All patients were followed at one week, one month, three months and six months subsequently.

At each follow-up, patient had BCVA charted, slit lamp biomicroscopy of anterior segment, IOP measurement and dilated fundus examination using +90DS lens. If IOP was found to be more than 21 mmHg, it was treated by topical anti-glaucoma medications. In case of uncontrolled IOP medically, Argon laser trabeculoplasty (ALT) and surgical procedure (trabeculectomy) were entertained.

For statistical purpose, Statistical Package for Social Sciences (SPSS) version 10.0 was used for data analysis. Frequency and percentages were computed for categorical variables including gender and diagnosis. Mean ± standard deviation was calculated for IOP and age. Repeated measures ANOVA was used to compare the significance of mean IOP at different follow-ups (1 week, 1 month, 3 months and 6 months) at 5% level of significance.

RESULTS

A total number of 150 patients (198 eyes) were included in the study. The distribution of patients with their diagnosis is shown in Table I.

Out of 150 patients (198 eyes), 82 were male (54.7%) and 68 were female (45.3%) (M: F = 1.2: 1). Mean age of patients was 50.61 ± 10.59 years ranging from 22 to 78 years. There were 58 right eyes (38.7%) and 44 left eyes (39.3%); both eyes were involved in 48 patients (32%) who consecutively received an intravitreal injection.

The IOP increased from 13.76 ± 2.79 mmHg to a mean of 15.73 ± 4.5 mmHg postoperatively after one week. After one month, IOP was increased to 17.3 ± 6.8 mmHg. After three months, IOP increased to 19.08 ± 8.6 mmHg and after six months IOP was 14.38 ± 4.9 mmHg ($p < 0.0001$).

A rise in IOP to the value higher than 21 mmHg was observed in 28 eyes (14.1%) {12 right, 8 left and 8 both eyes} after one week of IVTA. At one month follow-up, a rise in IOP was observed in 48 eyes (24.2%), {20 right, 14 left and 14 both eyes}. At three months follow-up, a rise in IOP was observed in 76 eyes (38.4%) {26 right, 24 left and 26 both eyes}. At six months follow-up, a rise in IOP was observed in 25 eyes (12.6%) {8 right, 11 left and 6 both eyes}. The elevation of IOP usually occurred after about 1-3 months (Figure 1).

Table I: Distribution of patients according to the diagnosis of 198 eyes (n = 150).

Diagnosis	Number of patients	Number of eyes	Raised IOP (76 eyes)
Diabetic maculopathy	68 (45.3%)	89 (44.9%)	26 (29.21%)
Branch retinal vein occlusion	24 (16%)	39 (19.7%)	16 (41.02%)
Uveitis	24 (16%)	24 (12.12%)	18 (75%)
Central retinal vein occlusion	22 (14.7%)	24 (12.12%)	12 (50%)
Age related macular degeneration	12 (8%)	22 (11.11%)	04 (18.18%)

Table II: Post IVTA intraocular pressure management and effects (n = 76).

Management		Number of eyes	Controlled	Uncontrolled
Beta blocker n = 36	Non-selective	34 (44.7%)	22 (61%)	14 (39%)
	Selective	02 (2.6%)		
Combination of beta blocker with carbonic anhydrase inhibitors n = 54 (40+14)	Topical	54 (71%)	36 (66.6%)	18 (33.34%)
Laser treatment n = 4	Argon laser (ALT)	04 (05%)	03 (75%)	01 (5%)
Surgical treatment n = 6	Trabeculectomy with MMC	06 (7.8%)	06 (100%)	00 (0%)

ALT = Argon laser trabeculoplasty; MMC = Mitomycin-C.

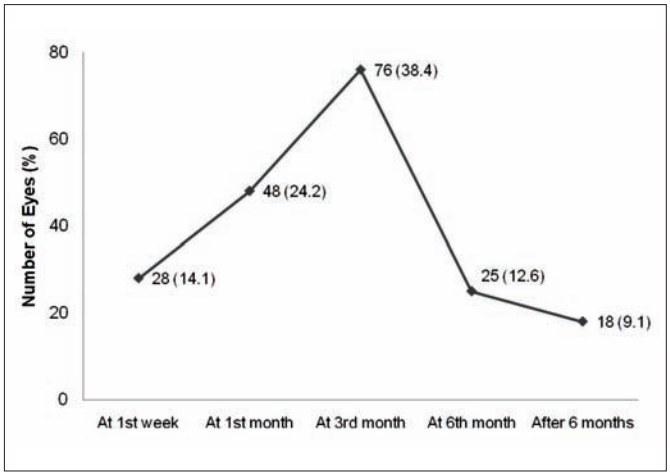

Figure 1: Frequency of IOP elevation following intravitreal triamcinolone acetonide (n = 198).

Twenty-six eyes (29.21%) with the pre-operative diagnosis of diabetic maculopathy demonstrated an IOP rise. Eighteen eyes (75%) with uveitis demonstrated an IOP rise. Twelve eyes (50%) with CRVO demonstrated an IOP rise. Out of 39 eyes with BRVO, IOP rise was seen in 16 eyes (41.02%), while in 22 eyes with ARMD IOP rise was seen in only 4 eyes (18.18%).

Out of 150 patients enrolled in the study, comprising of 198 eyes, 76 eyes (38.4%) required treatment to subside the increase in their IOP. Beta blockers were prescribed in 36 eyes (47%) and 34 were given non-selective timolol 0.5% (Blotim- Remington, Pak) and 2 were given selective betaxolol (Betoptic-S - Alcon, Belgium). The combination of beta blockers with carbonic anhydrase inhibitor was given in 54 eyes (71%) (Co-dorzal - Sante, Pak). ALT (Argon Laser Treatment) was performed in 4 eyes (5%) while trabeculectomy was carried out in 6 eyes (7.8%). Their outcome is given in Table II.

DISCUSSION

Intravitreal triamcinolone acetonide (IVTA) can be a therapeutical option for the treatment of various intraocular pathologies including neovascular, oedematous and proliferative diseases involving choroid and retina. It can also be used as an angiostatic agent in eyes with iris neovascularization, proliferative diabetic retinopathy and wet ARMD with presence of sub-retinal neovascular membrane (SRNVM).

Out of 198 eyes (150 patients), IVTA was given in 89 eyes (45.3%) of diabetic maculopathy and IOP was found to be raised in 26 eyes (29.2%), which is comparable to Selim and Ciardella's findings.[8,9] Selim *et al*. reported raised IOP in 35.7% eyes and Ciardella *et al*. reported raised IOP in 40% eyes of patients with diabetic macular oedema. In another study by Bashshur *et al*.,[10] out of 226 eyes, 59 eyes (26.1%) showed IOP measurements higher than 21 mmHg during follow-up. Similarly, in an study by Rhee and coworkers,[7] 528 eyes receiving single injections, 281 (53.2%) had an IOP elevation; 267 eyes (50.6%) experienced an elevation of IOP of at least 30%, and 245 (45.8%) and 75 (14.2%) eyes had an increase of 5 mmHg or 10 mmHg or more, respectively. In a study from Taiwan, there were 19 patients (36.5%) who experienced significant IOP elevation at a mean of 26.0 days after IVTA.[11] Lau and coworkers reported 64 (43.5%) of the 147 enrolled patients experiencing IOP elevation.[12] Ten patients (6.8%) had refractory IOP increase, and those 55 years of age or younger had a higher risk of refractory IOP elevation compared with those older than 55 years, with an odds ratio (OR) of 8.16 (p = 0.009), after adjusting for pre-operative IOP and diagnosis of retinal disease. Ansari also observed an IOP rise to values higher than 21 mmHg in 28 eyes (53.8%) of the English population.[13]

In this study, IVTA was used in 24 eyes of 22 patients (14.7%) of CRVO with IOP increasing in 12 eyes (50%) of 12 patients (54.5%). Cekio and co-workers observed raised IOP in 50% of their patients after IVTA was given due to macular oedema associated with CRVO.[14] In the present group of subjects with ARMD having SRNVM, post-injection rise of IOP was witnessed in 4 eyes (18.18%) of 12 patients (16.6% cases). Similar increase in IOP was observed by Chaudhary *et al*. in 40% cases.[15] In the present group of 39 eyes of 24 patients with BRVO, IOP elevation was seen in 16 eyes (41%). This is comparable to Jonas finding with similar diagnosis.[5] Out of 24 eyes of 24 patients with uveitis, IOP was elevated in 18 eyes of 18 patients (75%) after IVTA injection. Similar proportion of IOP elevation was reported by Tuncer and cowokers.[16]

The rise of IOP in our group of eyes was noticed at one week of post-injection period but peaked to highest level at 3 months and continued to show an increase for upto 6 months' post injection. At one month, post-injection rise of IOP was found in 24.2% of eyes, increasing to 38.4% at 3 months and in 12.6% eyes at 6 months' time. Ozkiris and Erkilic showed similar raised IOP occurring in 28.5%, 38.2% and 16.7% eyes at 1, 3 and 6 months respectively.[17] For this reason patient receiving IVTA should be monitored for a long-time to notice any change in IOP.

The potential benefits, easily availability and cost effectiveness makes triamcinolone acetonide, an attractive therapeutic agent to be used intravitreally in several choroidal and retinal vascular disorders. However, post-injection increase in IOP remains a serious concern almost seen in one-third of the patients. The rise in IOP is reported in almost similar fashion in patients with different racial backgrounds. Therefore, patients with history of glaucoma, family history of glaucoma and steroid responders are avoided to receive this drug. In a sub-group analysis, the biggest rise in IOP was noticed in the group with pan-uveitis, as some of these patients were also instilling topical prednisolone 1% which may be responsible for compounding the change in IOP. The age and gender were also found with no influence on rise of IOP.

CONCLUSION

After intravitreal triamcinolone acetonide, an IOP rise was observed in 38% eyes, starting about 1 to 6 months after the injection. In the vast majority, it was controlled by topical medication, but few patients required surgical intervention.

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