Original Research Article

Study of rise of intraocular pressure and effect on visual outcome in patients receiving intravitreal triamcinolone acetonide in macular disorders

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Abstract

Background: Macular edema represents a final common pathway response of the retina to a variety of possible insults. Intravitreal triamcinolone acetonide is commonly used in treatment of macular edema and hence complications associated with the treatment especially rise of IOP is common. Purpose: To find out the effect of Intravitreal injection of Triamcinolone Acetonide on IOP and visual outcome in various macular disorders. **Materials and methods:** It was a hospital based, prospective, non-randomised case study of 30 eyes of 30 patients receiving IVTA injections over duration of 1 year. **Results:** The mean pre-injection IOP was 14mmhg [11.7-16.3 mmHg]. The mean IOP at the end of 1 day, 1 week, 1 month and 3 month was 15.43mmhg, 17.53mmHg, 18.50mmhg and 16.40mmhg, respectively, with a maximum percentage change from the initial occurring at 1 month [31.9%]; the changes found to be significant. Majority [22 out of 30] of the patients in this study experienced a rise in IOP from baseline of upto 3-6 mmHg. The patients who experienced 3-6mmHg rise in IOP from baseline at 3 months follow up were treated with adequate control of IOP.In our study, there was significant improvement in visual acuity [Snellen's acuity improved by >/2lines] at the end of 1 and 3 months when compared with the initial visual acuity and visual acuity at the end of 1 week [p-value<0.001]. **Conclusion:** Intravitreal Triamcinolone Acetonide results in a significant rise in IOP which returns to initial baseline values within 3months of receiving treatment. Intravitreal Triamcinolone Acetonide results in a significant improvement in BCVA in patients diagnosed to have non-resolving macular oedema as a consequence of vascular and occlusive diseases of the retina.

Key Word: Diabetic retinopathy, Intravitreal triamcinolone acetonide, Intraocular pressure, Central retinal vein occlusion, Branch retinal vein occlusion, Best corrected visual acuity.

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INTRODUCTION

Triamcinolone acetonide is a synthetic, lipophilic corticosteroid with low solubility in aqueous solution, has been used as a depot drug for decades[1]. Its advantageous pharmacokinetic profile with rapid bioavailability and sustained release characteristics let Machemer to suggest the intravitreal use of crystalline triamcinolone acetonide to maintain therapeutic levels in the vitreous cavity[2].The safety of intravitreal triamcinolone administration has been supported by prior animal studies by MacCuen *et al*[3], and in human trials by Danis *et al*[4]. No toxic effect on the retina and optic nerve was observed. Intravitreal

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corticosteroids play an effective role in reducing inflammatory intraocular conditions. Chayen and associates demonstrated that histamine-induced disruption of lysosomes in skin tissue could be blocked by the synthetic glucocorticoid, fluocinolone. Consequently, it became widely accepted that the principal action of corticosteroids was the stabilization of lysosomal membranes[5].Macular edema represents a final common pathway response of the retina to a variety of possible insults. It is associated with vascular problems (such as diabetes and retinal vein obstruction), inflammatory conditions (such as pars planitis), inherited diseases (such as retinitis pigmentosa or dominant CME), tractional problems (such as vitreomacular traction syndrome), and medication use as in epinephrine (adrenaline) and following cataract surgery[6]. Currently intravitreal triamcinolone has been tried with variable success in Proliferative Diabetic Retinopathy, Cystoid Macular Edema in Central Retinal Vein Occlusion, Cystoid Macular Edema in Branch Retinal Vein Occlusion, Exudative Age Related Macular Degeneration, Diffuse Diabetic Macular Edema and Cystoid Macular Edema in chronic uveitis. Several side effects have been reported following intravitreal triamcinolone. Most common side effect being rise in IOP[7]. Others being Cataract[7], infectious and non-infectious endophthalmitis(Sutter and Gillis[8,9]). The purpose of our study was to determine the pattern of increase in the IOP following IVTA and to assess visual outcome in macular edema following IVTA.

AIMS AND OBJECTIVES

The objectives of this study were to find out the effect of Intravitreal injection of Triamcinolone Acetonide on Intraocular pressure. To find out the visual outcome following intravitreal injection of Triamcinolone Acetonide for macular edema's caused by various disorders of the eye.

MATERIALS AND METHODS

It was a hospital based, prospective, non-randomised case study of 30 eyes of 30 patients receiving IVTA injections over duration of 1 year. All patients were outpatients of the hospital. Detailed history was taken from all the patients. All patients needed to undergo a detailed clinical evaluation including Snellen's visual acuity testing, Slit lamp evaluation of the anterior segment, Fundus evaluation with indirect ophthalmoscope and Goldmann 3 mirror/ 90D lens., Goldmann's Applanation tonometry, Gonioscopy, Fundus photography, Fundus fluorescein angiography [F.F.A], Systemic evaluation.

Inclusion Criteria: Patients receiving IVTA injections

Exclusion Criteria: All patients with pre-existing causes for rise of IOP(known case of glaucoma).Patients who are known cases of steroid responsiveness. Written and informed consent were taken from all patients before the procedure. Eye lids and eye lashes were sterilized with 10% povidone iodine and a sterile eye speculum was placed. Ocular surface was sterilized by 5% povidone iodine. After installation of topical 4% Xylocaine, 4mg/0.1ml triamcinolone acetonide was injected into the vitreous cavity through the inferotemporal pars plana by using tuberculin syringe attached to a 26G needle in a sterile OT setting. A cotton tipped swap was pressed against the injection site to force the closure of the needle tract. Ocular massage was performed to normalize the IOP. Eye was examined for increase in IOP and paracentesis was done to lower the IOP whenever needed. The eye was bandaged and patients were suggested to hold their head in an upright position for the first 24 hour to avoid the precipitation of drug crystals over the macular region. Topical ofloxacin drop 5 times / day was used in all of the patients for 5 days. No repeat injection was done to the eyes. Patients were reviewed on post-operative day1, at the end of 1week, after 1 month and 3months thereafter .The responses to treatment were monitored functionally by visual acuity assessment. Clinical appearance of macular edema as seen by 3mirror/90 D lens was assessed. IOP was measured by applanation tonometry. Rise in IOP [>3 mmHg] at the end of 3 months follow up was treated with timolol eye drops 0.5% twice daily. Lenticular changes were assessed. Other possible adverse events were monitored. Descriptive statistical analysis has been carried out in the present study. Student t test has been used to find the significance of Visual acuity (based on sum of score) and IOP

RESULTS AND OBSERVATION

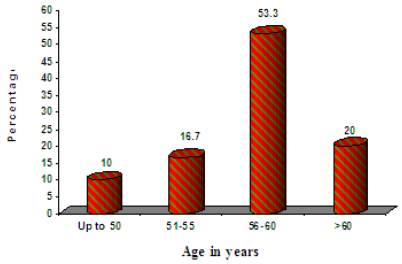

Figure 1: chart depicting the percentage distribution of patients based on age.

This chart shows the age wise distribution of patients included in our study. 53.3% of patients were between 56-60 years, 20% were above the age of 60 years, 16.7% were between 51-55 years and 10% 50 years and below.

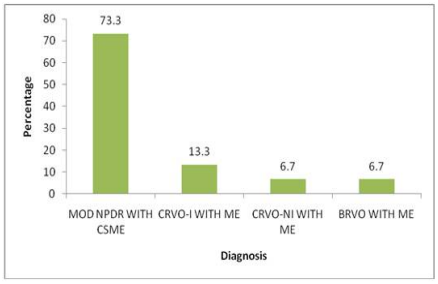

Figure 2: chart depicting the percentage distribution of patients based on the type of diagnosis.

The above graph depicts patient distribution based on the diagnosis in the eye receiving IVTA. 22(73.3%) had moderate NPDR with CSME, 4(13.3%) had CRVO – I with ME, 2(6.7%) had CRVO – NI with ME and 2(6.7%) had BRVO with ME. Majority of patients in our study had Mod NPDR with CSME.

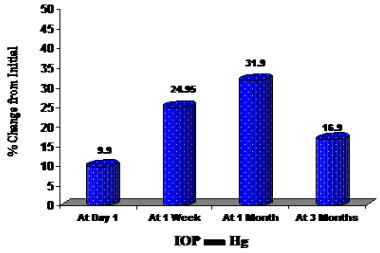

Figure 3: chart depicting percentage change of iop from the initial to different follow up periods.

The above chart shows the change in IOP from initial to different follow up periods. % change from initial (prior to IVTA) was maximum at 1 month i.e; 31.9% followed by 1 week i.e.; 24.95% and was least at 1st day i.e.; 9.9%.

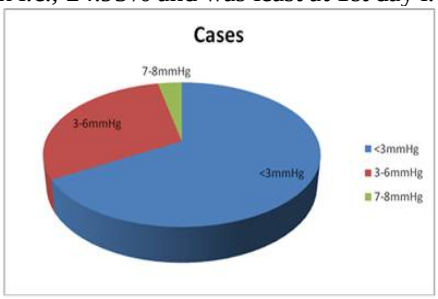

Figure 4: chart depicting ranges of increase in iop from the baseline in the study subjects at 3 months.

This chart shows majority of patients 20(66.7%) in our study had an IOP <3mmHg at 3 months and needed no treatment. But 9(30%) had 3-6mmHg and these 9 patients needed treatment with timolol 0.5% e/d BD and 1(3.3%) had IOP rise of 7-8mmHg and required treatment with timolol and dorzolamide. These 10 patients had IOP normalized after 1 month of treatment and required no further intervention.

Table 1: Effect of Intravitreal Triamcinolone Acetonide on Visual acuity at different follow up periods

Visual acuity	Initial	Day 1	Week1	Month 1	Month 3
6/6					
6/9			2(6.7%)	3(10.0%)	
6/12			6(20.0%)	6(20.0%)	4(13.3%)
6/18	2(6.7%)	2(6.7%)	8(26.7%)	4(13.3%)	8(26.7%)
6/24	6(20.0%)	5(16.7%)	9(30.0%)	11(36.7%)	6(20.0%)
6/36	9(30.0%)	12(40.0%)	3(10.0%)	3(10.0%)	8(26.7%)
6/60	10(33.3%)	11(36.7%)	2(6.7%)	3(10.0%)	4(13.3%)
5/60	1(3.3%)	-	-	-	-
4/60	2(6.7%)	-	-	-	-
3/60	-	-	-	-	-
2/60	-	-	-	-	-
HM+	-	-	-	-	-
PL and less	-	-	-	-	-
Mean +/- SD	7.60±1.19	7.93±0.91	9.77±1.33	9.47±1.80	8.93±1.26

Table 2: Line of improvement in BCVA (Best Corrected Visual Acuity) during the study Period [at different follow up visits]

Line of improvement in Visual acuity (n=30)	Month 1	Month3
1	16.7%	36.7%
2	56.7%	43.3%
3	20%	16.7%

At the end of 1month, 16.7% had 1 line improvement in BCVA, 56.7% had 2 line improvement and 20% had upto 3 lines of improvement. At month 3, 36.7%, 43.3% and 16.7% had 1, 2 and 3 lines of improvement in BCVA, respectively.

DISCUSSION

Glucocorticoids through stabilization of the blood brain barrier have been widely used for the treatment of brain edema. Because the blood retinal barrier is similar to the blood brain barrier, use of steroids in the treatment of macular edema is supported by the aboveeffects[10] Triamcinolone Acetonide by virtue of its stabilization of blood retinal barrier, anti-VEGF action and action at cellular levels has been proven to be effective management of various macular edemas including those not benefiting from Laser[11]. Venous obstructive disease of the retina and diabetic retinopathy, results in visual dysfunction through the presence of macular edema. These are the most common diseases associated with macular edema. Intravitreal triamcinolone acetonide (IVTA) has increasingly been applied as treatment for various intraocular neovascular and oedematous diseases. In our study, 30 patients [30 eyes] were diagnosed to have macular edema due to venous occlusive and vascular diseases of the retina. Intravitreal triamcinolone acetonide [4mg] was administered. Pre and post intervention, Best Corrected Visual Acuity [BCVA] and IOP was compared and analysed. In this study, 53.3% of patients were between the ages of 56-60years. The mean age was 59 years. 19 out of 30 patients were phakic, the remaining being pseudophakic.73.3% of patients had moderate NPDR with CSME, 13.3% had ischemic CRVO with macular edema 6.7% had non-ischemic CRVO with macular edema and 6.7% had BRVO with macular edema.86.7% of patients had predominant cystoid macular edema on FFA. In our study, there was significant improvement in visual acuity [Snellen's acuity improved by >/2lines] at the end of 1 and 3 months when compared with the initial visual acuity and visual acuity at the end of 1 week [p-value<0.001]. At the end of 1month, 16.7% had 1 line improvement in BCVA, 56.7% had 2 line improvement and 20% had upto 3 lines of improvement. At month 3, 36.7%, 43.3% and 16.7% had 1, 2 and 3 lines of improvement in BCVA, respectively. Around 74% of the patients had improvement in visual acuity of 1-2 lines at the end of 1 month. Around 80% of the patients had improvement in visual acuity of 1-2 lines at the end of 3 months. This may be due to factors like clearing of haemorrhages, formation of collaterals and subsequent reduction in the degree of ischemia along with the continued effect of IVTA namely stabilization of blood retinal barrier and reduction of effects mediated by various cytokines. In those patients whose visual acuity failed to maintain the 2 lines of improvement, the predominant diagnosis was that of ischemic maculopathy. One patient had a longer duration of symptoms of 10 months. These indicate the greater degree of ischemia and subsequent photoreceptor damage. A higher degree of macular edema for a longer duration can cause extensive damage to the photoreceptors. In 2 patients, V.A remained the same at 1and 3 months after intervention. In these patients the base line visual acuity was <6/60 and a longer duration of symptoms. This could be due to irreversible damage to the photoreceptors which precludes visual improvement. Patients with 3-4 lines of visual improvement had a better initial visual acuity and lesser duration of symptoms. Patel PJ *et al*[12] analysed the results of thirteen patients who received 4mg of intravitreal triamcinolone for the treatment of macular edema due to vein occlusions. Mean duration of symptoms before intravitreal triamcinolone acetonide injection was 6.8 months (SD 4.5 months). Eight eyes(62%) responded well with improved visual acuity and macular thickness 1–3 months postinjection. In our study, the mean pre-injection IOP was 14mmhg [11.7-16.3 mmHg]. None of the study subjects were a known case of glaucoma. The mean IOP at the end of 1 day, 1 week, 1 month and 3 month was 15.43mmHg, 17.53mmHg, 18.50mmHg and 16.40mmHg, respectively, with a maximum percentage change from the initial occurring at 1 month [31.9%]; the changes found to be significant. A majority [22 out of 30] of the patients in this study experienced a rise in IOP from baseline of upto 3-6 mmHg. The rise of IOP was independent of sex and diabetic status of the patients. The patients 9 patients who experienced 3-6 mmHg rise in IOP from baseline at 3 months follow up were treated with Timolol Maleate 0.5% eye drops twice daily, with adequate control of IOP. The patients who experienced7-8mmhg rise of IOP 1patient were treated with a combination of Dorzolamide and timolol, with adequate control of IOP. None of the patients required surgical management for the rise of IOP Park *et al*[13], The mean preinjection IOP was 15 mmHg (range, 9–18 mm Hg). Two eyes had a previous diagnosis of open-angle glaucoma. One patient (with a history of open-angle glaucoma on latanoprost) had an IOP elevation from 18 mm Hg (preinjection) to 45 mm Hg one month after the injection. The mean IOP was 14.6 mm Hg at 1 month post injection. The mean IOP at last follow-up for all eyes was 21.3 mm Hg ($P < .08$). Three eyes (30%) without previous history of glaucoma required initiation of topical aqueous suppressants for IOP control at last follow-up. In our study Progression of cataract was not quantified which is a known long term complication. None of our patients had post injection sterile endophthalmitis. IVTA can be chosen as primary treatment for predominant cystoid / diffuse with cystoid edema associated with various diseases of the retina, in accordance with various studies. A number of trials also advocate the combined use of IVTA and Macular Grid Laser for the treatment of macular edema[14].

CONCLUSION

Intravitreal Triamcinolone Acetonide results in a significant rise in IOP which returns to initial baseline values within 3 months of receiving steroid in majority of patients. Patients having high IOP even after 3 months were well controlled with topical antiglaucoma medications. Intravitreal Triamcinolone Acetonide results in a significant improvement in BCVA in patients diagnosed to have non-resolving macular edema as a consequence of vascular and occlusive diseases of the retina. It is particularly effective in Cystoid macular edema where laser is less effective. It can be tried as a primary modality of treatment in cystoid edema. It is an effective, cheap and relatively safe modality of treatment for non-resolving macular edema.

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