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Original Research Article

Outcome of intravitreal triamcinolone (IVTA) acetonide in various posterior segment disorder

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ABSTRACT

Aim: To study the response to the injection of intra-vitreal triamcinolone acetate (IVTA) in various indications and to identify the IOP rise between various groups.

Materials and Methods: An interventional, prospective study was conducted on 50 patients at vitreo-retinal department at tertiary eye hospital in Bangalore in the period of November 2015 to May 2017. Each patient was subjected to a detailed assessment which included patient's demographic data & detailed history. Best corrected visual-acuity (BCVA), Intra ocular pressure(IOP) was recorded. Macular oedema is confirmed by optical coherence tomography and fluorescein angiography. Patients that received injection IVTA were followed up for 6 months.

Results: The mean age of subjects was 56.78±10.76 years, 54% were males and 46% were females. In the study, 46% of eyes were diagnosed at CSME, 38% as BRVO, 8% as pseudophakic CME, 6% as CRVO and 2% as Uveitis. The mean BCVA LogMAR at baseline was 0.87±0.43 and at 6 months follow up mean BCVA LogMAR was 0.59 ± 0.42. In the study mean IOP at baseline was 14.24±3.01 and at 6 months follow up mean IOP was 15.12 ± 3.60. There was significant increase in IOP at 1 month follow up. The mean central macular thickness (CMT) at baseline was 469.4±138.4 and at 6 months follow up mean CMT was 290.9 ± 140.7.

Conclusion: Although there is a risk of raised IOP, IVTA can be preferred as a modality of treating macular edema as it has good results and is very economical and affordable.

1. Introduction

Posterior segment disorders constitute one of the important cause of visual disability. Among posterior segment disorders, macular oedema is a major cause of ocular morbidity. Here the blood brain barrier is disrupted; proteins and water enter retinal intracellular and extracellular space, leading to oedema. Macular oedema is diagnosed clinically by ophthalmoscope and confirmed by OCT (optical coherence tomography) and fluorescein angiography.[1]

Previously macular oedema was treated by laser photocoagulation, more recently intravitreal triamcinolone acetonide (IVTA) and anti-VEGF (anti-vascular endothelial growth factor) are the modalities of treatment.[2] IVTA has increasingly been used for treatment of intraocular oedematous, neovascular diseases, such as long standing macular oedema due to central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), diffuse diabetic macular oedema, proliferative diabetic retinopathy, chronic posterior uveitis, persistent pseudo-phakic cystoid

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macular oedema (CME), age related macular degeneration and other clinical conditions.[3] It has a half-life of 18.6 days and effects lasts up to 3 to 6 months with 4mg IVTA.[4] It is economical and easily available as compared to other anti -VEGF drugs.

This study describes the outcome of IVTA in various posterior segment disorders separately in terms of visual acuity, its effect on central macular thickness and also, we will study the intraocular pressure rise in various groups in whom IVTA is given.

2. Materials and Methods

A Hospital based time bound, interventional, prospective study was conducted on 50 patients who presented to the Vitreoretinal department of Regional Institute of Ophthalmology at Bangalore during the period of November 2015 to May 2017. Ethical clearance was obtained from the Institutional Ethical Committee.

Patients willing to give consent and retinal conditions like diabetic macular oedema, macular oedema in branch retinal vein occlusion and central retinal vein occlusion, exudative age-related macular degenerations, pseudo-phakic cystoid macular oedema, chronic posterior uveitis, cystoid macular oedema secondary to uveitis, etc were included in the study.

Patients with pre-existing glaucoma, already on systemic steroids for past 3 months, Family history of glaucoma, patients who have received previous intravitreal triamcinolone or anti-VEGF injection were excluded from the study. Also, patients with vitreomacular traction, epi-macular membrane, thickened posterior hyaloid attached at macula were excluded as OCT imaging was challenging were excluded.

Patients underwent detailed ocular examination including Visual acuity by Snellen's chart and near vision chart, anterior and posterior segment evaluation, IOP measurement using Goldmann applanation tonometer and glaucoma evaluation. Fundus examination using indirect ophthalmoscope, slit lamp bio-microscopy with 90D lens. SD-OCT was done to measure central foveal thickness. Vertical retinal cross-sections with the instrument centered on the fovea and using the macular 512*128 scan protocol was followed.

During each follow up, best corrected visual acuity using snellen's chart, IOP was measured using Goldmann applanation tonometer and OCT was done.

2.1. Technique of IVTA injection

The procedure is carried out under aseptic precautions in a sterile OT setup under topical anaesthesia. The stab is given 3-3.5mm from the limbus in aphakic and pseudo-phakic eyes and 3.5-4mm mm from the limbus in phakic eyes usually infero-temporally. The 26 G needle is directed towards the centre of the globe. Using a single purposeful continuous manoeuvre 0.1 ml (4mg) triamcinolone acetonide is injected into the eye. Eye is examined for increase in IOP and paracentesis is done to lower the IOP. Post operatively patients were put on topical moxifloxacin drops 6 times per day.

Patients are reviewed on post-operative day one, at the end of one week, after one month, three months and six months.

Data was entered into microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean and standard deviation. Paired t test is the test of significance for paired data such as before and after treatment for quantitative data. p value (Probability that the result is true) of <0.05 was considered as statistically significant.

3. Results

The mean age of subjects was 56.78 ± 10.76 years Chart 1, majority of subjects were in the age group 61 to 70 years (32%). In the study 54% were males and 46% were females.

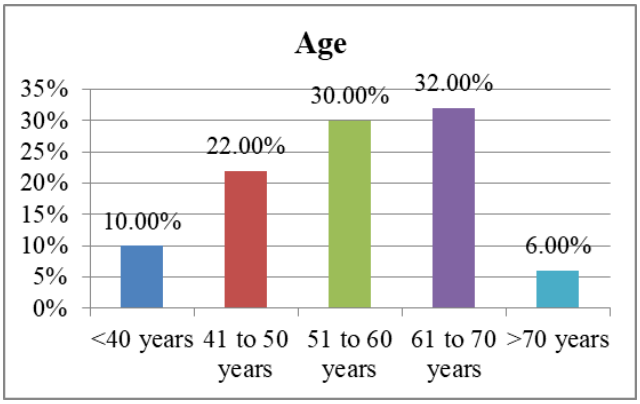

Chart 1: Showing age distribution of subjects

Mean duration of symptoms 4.3 ± 2.4 months Chart 2. Majority of subjects had symptoms for 4 to 6 months (36%). In the study, 46% of eyes were diagnosed at cystoid serous macular oedema (CSME), 38% as branched retinal vein occlusion (BRVO), 8% as Pseudo-phakic cystoid macular odema (CME), 6% as central retinal vein occlusion (CRVO) and 2% as Uveitis. Table 1

3.1. Change in BCVA

The mean BCVA Log MAR at baseline was 0.87 ± 0.43 and at 6 months follow up mean BCVA Log MAR was 0.59 ± 0.42. There was significant decrease in BCVA Log MAR (i.e. improvement in vision) from 1 month follow up to 6 months compared to baseline values. (Table 2)

Table 1: Diagnosis among subjects. CSME- Cystoid serous macular oedema, BRVO- Branched retinal vein occlusion, CME- Cystoid macular oedema, CRVO- Central retinal vein occlusion

		Count	%
Diagnosis	CSME	23	46.0%
	BRVO	19	38.0%
	Pseudo-phakic CME	4	8.0%
	CRVO	3	6.0%
	Uveitis	1	2.0%
	Total	50	100.0%

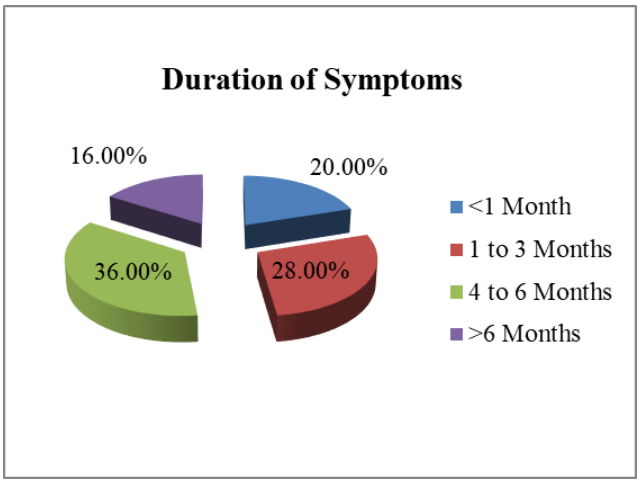

Chart 2: Showing duration of symptoms among subjects

In the CSME group, there was significant decrease in BCVA Log MAR (i.e. improvement in vision) after 4mg IVTA treatment compared to baseline values. BCVA reduced from 0.87 to 0.73.

Similarly, in BRVO group there was significant decrease in BCVA Log MAR (i.e. improvement in vision) after 4mg IVTA treatment compared to baseline values. BCVA reduced from 0.92 to 0.42. Decrease in BCVA Log MAR was highest for BRVO group than any other group. In CRVO group there was increase in mean BCVA Log MAR at all the intervals of follow up compared to baseline but was not statistically significant.

Table 2: CVA Log MAR at different periods of follow up.

BCVA Log MAR	N	Mean	SD*	P value
Baseline	50	0.87	0.43	
1 Week	50	0.87	0.43	-
1 Month	50	0.64	0.38	<0.001*
3 Months	50	0.58	0.38	<0.001*
6 Months	50	0.59	0.42	<0.001*

*Standard deviation.

3.2. *Changes in IOP*

In the study mean IOP at baseline was 14.24 ± 3.01 and at 6 months follow up mean IOP was 15.12 ± 3.60. There was significant increase in IOP at 1 month follow up. IOP gradually decreased at 6 months follow up as compared to first month and third month values. (Table 3)

Table 3: IOP at different periods of follow up

IOP	Count	Mean	SD	P value
Baseline	50	14.24	3.01	
1 Week	50	14.20	2.81	0.886
1 Month	50	17.02	5.82	<0.001*
3 Months	50	15.92	5.08	0.003*
6 Months	50	15.12	3.60	0.038*

Mean IOP comparison at different intervals of Follow up with respect to Diagnosis

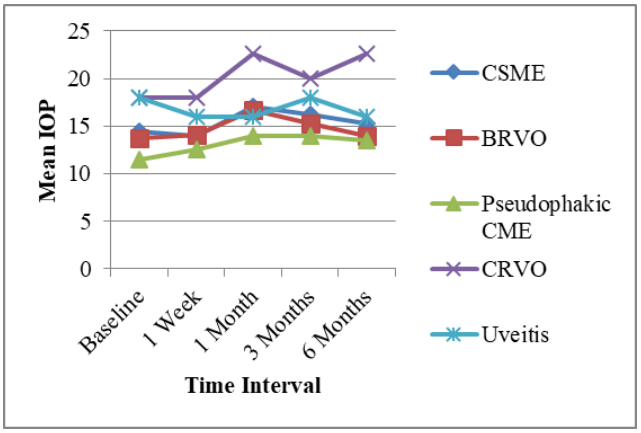

Chart 3: Line diagram showing Mean IOP comparison at different intervals of Follow up with respect to diagnosis

However, there was no significant difference in mean IOP in CSME, BRVO, pseudophakic CME and CRVO group at all the intervals of follow up compared to baseline values except for BRVO at 1 month. (Chart 3)

3.3. *Change in CMT*

The Mean CMT at baseline was 469.4 ± 138.4 and at 6 months follow up mean CMT was 290.9 ± 140.7. There was significant decrease in CMT from 1 month follow up to 6 months compared to baseline values. There was significant difference in mean CMT in CSME, BRVO, Pseudophakic CME and CRVO group at all the intervals of follow up compared to baseline values except for Pseudophakic CME at 6 months. (Table 4, Chart 4)

The most frequent immediate post op complications in the study was sub-conjunctival haemorrhage (26%) followed by anterior uveitis (10%)

At one month follow up raise IOP was present in 9 subjects out of 50 of those who received IVTA. Progression

Table 4: Mean CMT comparison at different intervals of Follow up with respect to diagnosis CSME- Cystoid serous macular oedema, BRVO- Branched retinal vein occlusion, CME-Cystoid macular oedema, CRVO- Central retinal vein occlusion, SD- standard deviation.

CMT	Diagnosis											
	CSME			BRVO			Pseudophakic CME			CRVO			Uveitis	
	Mean	SD	P value	Mean	SD	P value	Mean	SD	P value	Mean	SD	P value	Mean	SD
Baseline	476.30	103.34		437.32	99.94		471.00	124.24		691.00	361.35		250.00	.
1 Month	332.70	128.29	<0.001*	291.53	85.88	<0.001*	316.00	49.72	0.028*	580.33	379.58	0.039*	199.00	.
3 Months	307.91	127.20	<0.001*	239.28	58.66	<0.001*	257.00	37.43	0.049*	540.33	412.80	0.038*	186.00	.
6 Months	311.48	124.80	<0.001*	242.16	67.08	<0.001*	260.00	76.80	0.089	518.67	388.83	0.01*	184.00	.

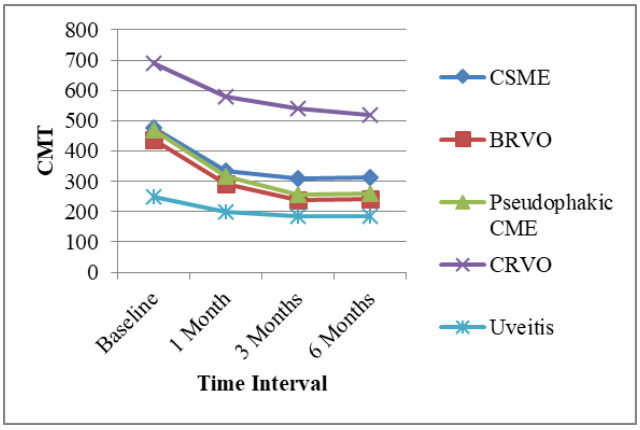

Chart 4: Line diagram showing Mean CMT comparison at different intervals of Follow up with respect to diagnosis

of cataract was observed in 10% individuals.

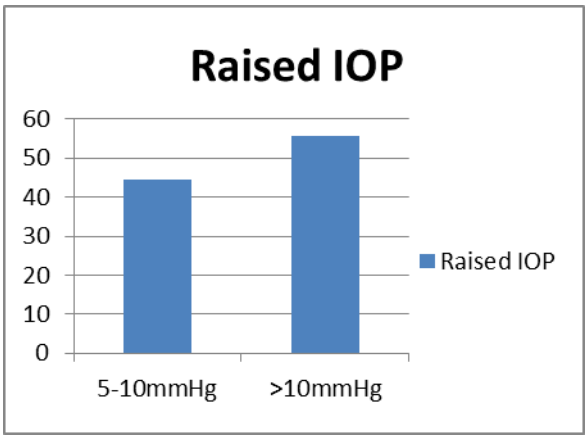

Chart 5: Showing raised IOP during follow up

Minimal or No improvement with IVTA (4mg): Chart 6 showing subjects showing no improvemet on IVTA.

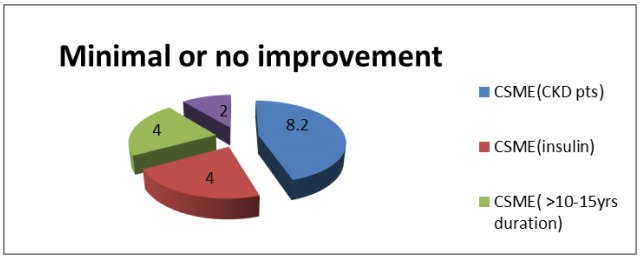

Chart 6: Showing cases with no improvement on IVTA

A total of 14% of subjects has recurrence in macular oedema after initial resolution of oedema.

Table 5: Recurrence of cystoid oedema at 6 month follow up. CSME- Cystoid serous macular oedema, BRVO- Branched retinal vein occlusion

Diagnosis	No of patients	%
CSME	3	6%
BRVO	3	6%
Pseudo-phakic cystoid oedema	1	2%
Total	7	14%

4. Discussion

In our study, we demonstrate the outcome and efficacy of IVTA in various posterior segment disorders which include Diabetic CSME, macular edema secondary to BRVO and CRVO, pseudo-phakic cystoid macular edema and uveitis. IVTA stabilizes the blood retinal barrier and has anti-VEGF action. It acts at cellular level, thus been proven effective in management in macular edema.

Our study is a prospective, non-randomized interventional clinical study of 50 eyes of various posterior segment disorders who received intravitreal triamcinolone acetonide injection (4mg) in South India in Indian subjects. The patients were followed up at 1 week, 1 month, 3 months and 6 months and were evaluated under the following which include BCVA(Log MAR), central macular thickness(CMT), intraocular pressure(IOP) and grading of cataract.

In our study most of the patients were of age group 51-60yrs and 61-70 years (30% and 32% respectively). Gender distribution was almost similar of 54% males and 46% females. The mean duration of symptoms was 4.3±2.4 months. Majority of individuals had symptoms for 4-6 months (36%). 29 patients were diabetic and 27 were hypertensive.

In our study, after IVTA was administered for Macular edema on follow up there was a significant decrease ($p<0.001$) in BCVA Log MAR from baseline of 0.87±0.43 to 0.58±0.38 and 0.59±0.42 at 3 and 6 months respectively.

There was also a significant decrease in CMT ($p<0.001$) from baseline mean CMT 469±138.4 to 290±145.5 at 3 months and 290.9±140.7 at 6 months.

Out of 50 eyes that received IVTA, 23 of them had diabetic CSME, 19 eyes with macular edema secondary to BRVO, 4 eyes with pseudo-phakic macular edema, 3 with CRVO and 1 eye with uveitis.

Considering each group, in CSME group, there was significant decrease in BCVA log MAR (i.e. improvement in vision) after 4mg IVTA. BCVA reduced from mean of 0.87 to 0.73 and there was significant reduction in CMT from mean thickness of 476.30±103.4 to 311.48±124.80. These values are comparable to the study performed by Norlaili et al who injected 4mg Triamcinolone acetonide Intravitreally into 40 eyes with diabetic macular edema as primary treatment. The mean visual acuity improved from 0.93±0.2 at baseline to 0.40±0.2 at three months follow up.[5]

Sallam et al found proportional improvement in macular edema but effect was transient and necessitating repeat injections in patients with CSME.[6] In our study 3 eyes out of 23 eyes with CSME needed repeat injection as there was transient decrease in CMT as long as the effect of triamcinolone acetonide lasted, after which macular edema increased and at 6 months follow up patient was advised for a repeat injection.

Five patients with CSME who also had chronic kidney disease (CKD) were found to be 5 in number. Out of these, 2 patients (40%) showed minimal or no improvement with IVTA and 2 eyes (40%) needed repeat injection at six months follow up.

In our study 4 mg IVTA was given to 19 eyes with macular edema secondary to branch vein occlusion (BRVO). Out of which, in 14 eyes (73.68%) supero-temporal quadrant was affected, in the rest inferotemporal quadrant was affected (26.3%). Increased incidence in supero-temporal quadrant is thought to increase number of arteriovenous crossing in that quadrant. The Eye Disease case control study and Beaver Dam Eye study also reported similar observation. Incidence of BRVO is most common in supertemporal quadrant (58-66%) followed by inferotemporal (29%) and least common in nasal quadrant (2.9%). In our study majority of patients had visual acuity of < or = 6/60(58%) and 8 out of 19 eyes had < or =6/18 visual acuity.[7,8] Pre injection mean BCVA Log MAR was 0.92±0.35 and statically significant improvement was found at 1 month, 3 months and 6 months($p<0.001$) 0.53±0.36, 0.40±0.34,0.42±0.36 respectively. There was better improvement in BCVA at 3 month follow up.

In a similar study by Cheng et al, mean Log MAR visual acuity at presentation was 0.77±0.43 which was comparable to ours. At 4 month follow up BCVA improved significantly from 0.77±0.43 to 0.44±0.43 log MAR.[9] In our study we followed up patients until 6 months and the results were comparable. In a study by Zhao et al, mean BCVA was 45.65±19.01 at presentation was which was comparable to ours. At 6 month follow up BCVA improved significantly from 45.65±19.01 to 58.82±17.31.[10]

Assessment of baseline CMT of patients in our study showed a mean CMT of 437.32±99.94 at initial presentation. At 1 month follow up post IVTA, CMT reduced in all patients to a mean value of 291.53±85.88 which was statistically significant ($p<0.001$). Mean CMT further reduced at 3 months follow up to 239.28±58.66 and remained constant in most cases or there was a minimal increase in CMT at 6 months follow up.

Jonas et al conducted a non-randomized comparative study on 11 eyes with CRVO and found that there was a gain in visual acuity which was significant ($p=0.003$).[11] This study also showed that the improvement in visual acuity was transient. In our study that included 3 eyes with CRVO

although there was a slight reduction in CMT, there was no improvement in visual acuity.

Among 4 eyes with pseudo-phakic cystoid macular edema post small incision cataract surgery in our study, mean BCVA Log MAR was 0.65±0.54 which improved at follow up to 0.43±0.20 at 3 months and to 0.40±0.36 at 6 months follow up. There was a reduction in CMT from 471±124.25 to 260±168 at 6 months follow up that was significant (p=0.47).

A study by Jonas et al included five patients suffering from cystoid macular odema after cataract surgery who received an intravitreal injection of 25-mg triamcinolone acetonide. In the follow-up period of 6.6 +/- 4.1 months, visual acuity increased from 0.26 +/- 0.13 to a mean maximal visual acuity of 0.60 +/- 0.19. For all patients, visual acuity improved during the follow-up by at least 0.20 which is comparable to our study.[12]

5. Discussion

None of the patients had a baseline IOP more than 20mmHg. Mean IOP was 14.24±3.01. 9 out of 50 patients had raised IOP in our study. Out of 9 patients, 4 had IOP rise from baseline IOP greater than 10mm Hg and 4 had IOP rise more than 5-10mmHg from baseline IOP. One patient with CRVO ended up with neovascular glaucoma and raised IOP. Mean IOP at 1 month follow up was 17.02±5.82 mm Hg and was statistically significant (p<0.001). At 6 months follow up, mean IOP was 15.12±3.60. This shows that IOP reduces once IVTA crystals disappears from vitreous cavity. Patients with raised IOP were managed with topical anti glaucoma medication. None of them required surgery. J.B Jonas et al showed that intraocular pressure increased significantly from mean 15.43 to a mean maximum 23.38mm Hg post operatively. A rise in IOP to values higher than 21mm Hg was observed in 39(52%). IOP elevation occurred after 1-2 month.[13] This study showed greater IOP elevation compared to our study and be because of use of a higher dose 20mg. V Rajshekar et al showed that intraocular pressure increased significantly from mean 15.6mmhg to a mean maximum 20.8mmhg and 19.2mm Hg post operatively at first and three months postoperatively.[14]

In our study progression of cataract post IVTA was found in 5 patients (10%). Also, there were 5 cases of anterior uveitis that was managed with topical antibiotics and cycloplegic drugs. None of our patients had retinal detachment of vitreous haemorrhage.

There was recurrence of macular edema in 14% individuals which constitutes 7 out of 50 patients during follow up.

Grzybowski A et al reviewed various treatment updates for macular oedema in vascular retinal diseases. He concluded that intravitreal steroids do have increased functional and anatomical outcomes and the side effects could be due to preservatives.[15]

6. Conclusion

Intravitreal triamcinolone acetonide 4mg is effective in improvement of vision and reduction in central macular thickness in diabetic CSME, macular edema secondary to BRVO and pseudo-phakic cystoid macular edema and not very effective in macular edema due to CRVO. Most cases of raised IOP normalize at 6 months and can be controlled by topical antiglaucoma medication. Patients with diabetic CSME also having CKD don't respond very well to IVTA or may have higher recurrence of macular edema. A larger study series might be needed to evaluate the effectiveness in these cases.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

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