Original Research Paper

Volume-10 | Issue-1 | January - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Ophthalmology

ROLE OF INTRAVITREAL TRIAMCINOLONE IN DIABETIC MACULAR EDEMA

Dr. Renu Dhasmana — Professor and Head, Department of ophthalmology, Himalayan Institute of Medical Sciences, SRHU, Jolygrant, Dehradun, Uttarakhand

Dr. Harsh Bahadur — Professor, Department of ophthalmology, Himalayan Institute of Medical Sciences, SRHU, Jolygrant, Dehradun, Uttarakhand

Dr. Darshika Rawat* — Senior Resident, Department of ophthalmology, Himalayan Institute of Medical Sciences, SRHU, Jolygrant, Dehradun, Uttarakhand *Corresponding Author

ABSTRACT

Purpose: To evaluate the effect of intravitreal triamcinolone in diabetic macular edema.

Methods: All diabetic patients presenting to ophthalmology OPD of a tertiary care hospital in Uttarakhand over a period of one year, fulfilling the inclusion and exclusion criteria, were included in the study. Detailed eye examination, pre-injection FFA and OCT was done. Single IVTA injection was given to proven cases of diabetic macular edema and patients were examined for improvement of vision and change in macular thickness, at 6 and 12 weeks interval.

Results: Total 30 patients were included. There was increase in BCVA in the study group. There was significant decrease in macular thickness in all three groups at 6 weeks and 12 weeks (p=0.0015). Post injection the macular thickness reduced and BCVA improved, thus proving IVTA to be effective in the treatment of DME.

Conclusion: the study showed that triamcinolone acetonide is an effective treatment of DME.

KEYWORDS : diabetic macular edema, IVTA

INTRODUCTION

Over the last decade, management of diabetic macular edema (DME) has undergone a paradigm change (1). Newer diagnostic tools and pharmacological agents have contributed to better understanding and management of the condition (2). The prevalence of DME in patients with diabetic retinopathy is 2.7% – 11% (3). The incidence of DME in 10 years, was 20.1% in patients with type I diabetes mellitus, 13.9% in patients with type 2 diabetes using insulin, and 25.4% in type 2 diabetics not using insulin as described in the WESDR (Wisconsin Epidemiologic Study of Diabetic Retinopathy) (3). Several studies have demonstrated the role of inflammation in diabetic retinopathy (DR) and DME. Both VEGF and non-VEGF pathways contribute significantly to DME. Several studies on steroids for treatment of DME have been undertaken to study their anti-inflammatory and anti-edematous effects. There is inhibition of arachidonic acid pathway by corticosteroids, via phospholipase A2 blockage. This further blocks the synthesis of leukotrienes, prostaglandins and thromboxanes, preventing vasodilation and increasing the permeability of capillaries. Also these agents stabilize the lysozymes and blood retinal barrier (BRB), decrease inflammatory mediators and VEGF synthesis and inhibit cell proliferation. Corticosteroids are found to increase the number as well as the activity of tight junctions in the retinal capillary endothelium, which improves the oxygenation of retina (4). Management of DME broadly involves metabolic control of diabetes mellitus and co-morbid conditions along with non-steroidal anti-inflammatory drugs (NSAIDs), laser, intra-vitreal Anti-VEGF agents and steroids (2). In a study by Sonoda et al. it was found that within an hour of IVTA, the central macular thickness decreased significantly while, no change was seen with injection bevacizumab till post-operative day one (5). Failure to respond to anti-VEGF therapy may be defined as no anatomic improvement or a recurrence of retinal exudation on extending the interval between injections. Steroid therapy should be considered in all such cases (6). Steroids for the treatment of DME can be delivered in the form of posterior subtenon injection, peribulbar and intravitreal injection, or intravitreal implant. Currently, three different steroids are used intravitreally: triamcinolone acetonide, dexamethasone and fluocinolone acetonide (7). IVTA in suspension form is currently available as the following commercial preparations: Kenacort (Bristol-Myers-Squibb, Melbourne, Australia), Kenalog (Bristol-Myers-Squibb, Princeton, NY, USA) and Trivaris (Allergan, Irvine, CA, USA) (8). In India, available commercial preparations are: Aurocort, Tricort and Kenacort. The commonest side effects of intravitreal steroids are elevated intraocular pressure (IOP) and cataract formation (9). Currently, the intravitreal injection triamcinolone acetonide is used off-label to treat DME. It is recommended either alone or with laser therapy in patients with refractory DME and vision loss, particularly pseudophakic patients (10). Also, steroids prove to be useful in pregnant patients having DME. They have shown to reduce the number of injections as well as the cost of the treatment, thus increasing patient compliance and satisfaction. This study was conducted to assess the efficacy of IVTA on visual acuity and macular thickness, at a tertiary care hospital of Uttarakhand, in diabetic patients suffering from DME.

MATERIAL AND METHODS:

All patients of DME, attending eye OPD of Himalayan Institute of Medical Sciences, Utarakhand, over a period of 12 months and who did not receive any treatment for it in last 4 months, were included in the study. Patients with uncontrolled diabetes mellitus, hypertension, cardiac or renal disease, concurrent ocular disease such as retinal vein occlusion, uveitis, hazy media interfering with fundus evaluation, glaucoma suspects, established glaucoma patients, or patients requiring surgery within 3 months of enrollment were excluded. After detailed history and examination, pre-injection fundus fluorescein angiography (FFA) was done to classify the type of macular edema, optical coherence tomography (OCT) macula was done to assess the macular thickness. Single IVTA injection was given to all proven cases of diabetic macular edema. A total of 49 eyes of 30 patients were included in the study and patients were examined after treatment to look for improvement in vision and change in macular thickness, noted clinically and confirmed by FFA and OCT at 6 and 12 weeks interval.

RESULTS:

Of total 30 patients, 18 were males and 12 were females. Study group was further divided into three groups on the basis of foveal thickness on OCT as: Group I (200-400µm), Group II (401-600µm), Group III (>600µm). Maximum number of patients had a BCVA value with in 6/18-6/24 range (69.4%). Out of 49 eyes, 11 were phakic and 38 were pseudophakic. The mean pre-injection macular thickness in the study group was 505.12 (+/- 128.7) µm.

Table 1 shows BCVA at 6 weeks and 12 weeks post IVTA. Overall, post injection, there was increase in BCVA in the study group. On comparing the macular thickness in different groups, after giving a single injection of IVTA, it was found to decrease significantly in all the three groups, at 6 weeks and 12 weeks (p=0.0015), as shown in table 2.

Table 1: BCVA at 6 weeks and 12 weeks post IVTA

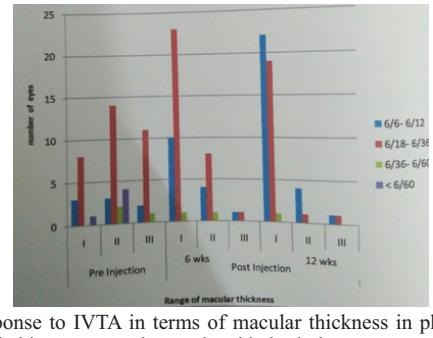
BCVA	6 Weeks			12 Weeks		
	Number of eyes	%	Mean	Number of eyes	%	Mean
6/6-6/12	15	30.61	0.34±0.09	26	53.06	0.36±0.07
6/18-6/24	32	65.31	0.59±0.07	22	44.89	0.58±0.10
6/36-6/60	2	4.08	0.85±0.07	1	2.04	0.8
<6/60	0	-	-	0	-	-
Total	49	100	0.52±0.16	49	100	0.52±0.18

Table 2: Macular thickness post IVTA observed on OCT

Group	6 weeks			12 weeks		
	Number of eyes	%	Mean macular thickness (µm)	Number of eyes	%	Mean macular thickness (µm)
I	34	69.39	300.85±53.48	42	85.71	223±32.49
II	14	28.57	492.15±53.49	5	10.21	500.6±66.77
III	1	2.04	702.5±45.96	2	4.08	709.5±36.06

Correlation between pre and post- injection BCVA and macular thickness (shown in figure 1), was assessed and it was found that as the macular thickness reduced, the BCVA improved, thus indicating the effectiveness of the injection (r value = -0.29, p value = 0.0026).

Figure 1: Correlation between pre and post-injection BCVA and macular thickness



The response to IVTA in terms of macular thickness in phakic and pseudophakic eyes was observed and in both the groups, a significant decrease in the macular thickness was found. In phakic eyes pre injection macular thickness was 540.9 µm which decreased to 245 µm at 12 weeks. In pseudophakic eyes, pre injection mean macular thickness was 493.34 um, which decreased to 279.3 µm at 12 weeks. In phakic eyes, reduction in macular thickness was more as compared to pseudophakic eyes (p value = 0.021), shown in table 3. Table 4 shows the BCVA after injection IVTA in phakic and pseudophakic eyes.

Table 3: Response to injection IVTA in terms of macular thickness in Phakic and Pseudophakic eyes

Group	Phakic eyes			Pseudophakic eyes		
	At presentation	At 6 weeks	At 12 weeks	At presentation	At 6 weeks	At 12 weeks
I	3	6	10	9	28	32
II	3	5	1	19	8	4
III	5	0	0	10	2	2
Mean	540.9	388.02	245	493.34	364.84	279.34
Standard deviation	138.5	147.07	113.85	125.75	127.07	138.35

Table 4: BCVA after injection IVTA in phakic and pseudophakic eyes.

BCVA	Phakic eyes			Pseudophakic eyes		
	At presentation	At 6 weeks	At 12 weeks	At presentation	At 6 weeks	At 12 weeks
6/6-6/12	2	3	4	6	12	23
6/18-6/24	5	6	7	28	26	14
6/36-6/60	1	2	0	2	0	1
<6/60	3	0	0	2	0	0
Mean BCVA	0.56±0.26	0.6± 0.16	0.54± 0.15	0.62± 0.26	0.50± 0.14	0.44± 0.16

DISCUSSION

Diabetic macular edema is found to be the most common cause of persistent vision loss, second only to vitreous or pre-retinal hemorrhage (11). IVTA has shown promising results in various studies conducted all over the world, for the treatment of refractory DME. Steroids have been proved to be useful in pseudophakic patients showing poor response to intra-vitreal anti-VEGF injections and in pregnant patients. Also, steroid injections are a cheaper modality of treatment and reduce the number of injections compared to anti-VEGF injections (12). In present study, there was increase in BCVA in the study group. The macular thickness in different groups, post-injection IVTA, decreased significantly at 6 weeks and 12 weeks. On correlating pre and post- injection BCVA and macular thickness, it was observed that as the macular thickness reduced and the BCVA improved, thus proving the effectiveness of the injection.

Various clinical trials have been undertaken to assess the efficacy of IVTA in the treatment of DME. A study by Jonas et al was conducted to compare 10 DME patients without a history of laser in the past to a group of 16 controls who had undergone previous laser photocoagulation. It was found that there was no significant change in visual acuity in both the groups at the end of 3 months follow-up (13). Maasim et al also found a significant reduction in the central macular thickness in the eyes of patients not responding to laser compared to control eyes. But the study observed that the effect did not last more than 24 weeks as the DME recurred (14).

Landmark study by Martidis et al on 16 eyes with CSME, not responding to at least 2 previous sessions of laser photocoagulation, showed improvement in vision and decreased macular thickness on OCT after IVTA (15). Study by Ahmed et al was conducted in 42 eyes, to evaluate the outcome of IVTA in DME. The study found the mean visual acuity improved by 0.02 logMAR units, while the central subfield thickness improved by 18.36 um at the end of 6 months post IVTA (16). Ozkan et al showed that post bevacizumab injection there was more rapid and frequent recurrence of macular edema compared to those with injection IVTA (17). Liu et al compared the efficacy of IVTA and intravitreal bevacizumab (IVB) for treating CSME and showed that IVTA was better than IVB in reducing central retinal thickness and in improving BCVA (18).

The limitation of the present study was a small sample size and a short follow-up period. Further studies on long term safety and efficacy of IVTA and complications of repeated injection of IVTA are required.

CONCLUSION:

The current study showed that triamcinolone acetonide is an effective treatment for DME. Post injection, eyes showed improved visual acuity and reduction of macular thickness.

REFERENCES

1. Arevalo, J. F. (2014). Diabetic macular edema: changing treatment paradigms. Current opinion in ophthalmology, 25(6), 502-507.
2. Raman R, Bhende M. Diabetic Macular Edema. Medical & Vision Research Foundations. 2015 Jun;33(2):50.
3. Browning, D. J., Stewart, M. W., & Lee, C. (2018). Diabetic macular edema: Evidence-based management. Indian journal of ophthalmology, 66(12), 1736.
4. Klein, R., Klein, B. E., Moss, S. E., & Cruickshanks, K. J. (1995). The Wisconsin epidemiologic study of diabetic retinopathy XV: the long-term incidence of macular edema. Ophthalmology, 102(1), 7-16.
5. Stewart, M. W. (2012). Corticosteroid use for diabetic macular edema: old fad or new trend?. Current diabetes reports, 12(4), 364-375.
6. Sonoda, Y., Arimura, N., Shimura, M., & Sakamoto, T. (2011). Early change of central macular thickness after intravitreous triamcinolone or bevacizumab in diabetic macular edema or retinal vein occlusion. Retina, 31(2), 290-297.
7. Tabakcı, B. N., & Ünlü, N. (2017). Corticosteroid treatment in diabetic macular edema. Turkish journal of ophthalmology, 47(3), 156.
8. Zhang, X., Zeng, H., Bao, S., Wang, N., & Gillies, M. C. (2014). Diabetic macular edema: new concepts in patho-physiology and treatment. Cell & bioscience, 4(1), 27.
9. Bhagat, N., Grigorian, R. A., Tutela, A., & Zarbin, M. A. (2009). Diabetic macular edema: pathogenesis and treatment. Survey of ophthalmology, 54(1), 1-32.
10. Bandello, F., Preziosa, C., Querques, G., & Lattanzio, R. (2014). Update of intravitreal steroids for the treatment of diabetic macular edema. Ophthalmic research, 52(2), 89-96.
11. Abraldes, M. J., Fernández, M., & Gómez-Ulla, F. (2009). Intravitreal triamcinolone in diabetic retinopathy. Current diabetes reviews, 5(1), 18-25.
12. Taylor, S. C., Montana, C., Shah, M., & SApte, R. (2018). Diabetic Macular Edema. Retina: Medical & Surgical Management, 309.
13. Jonas, J. B., & Degenring, R. (2002). Intravitreal injection of crystalline triamcinolone acetonide in the treatment of diffuse diabetic macular oedema. Klinische Monatsblatter fur Augenheilkunde, 219(6), 429-432.
14. Massin, P., Audren, F., Haouchine, B., Erginay, A., Bergmann, J. F., Benosman, R., ... & Gaudric, A. (2004). Intravitreal triamcinolone acetonide for diabetic diffuse macular edema: preliminary results of a prospective controlled trial. Ophthalmology, 111(2), 218-224.
15. Martidis, A., Duker, J. S., Greenberg, P. B., Rogers, A. H., Puliafito, C. A., Reichel, E., & Baumal, C. (2002). Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology, 109(5), 920-927.
16. Al Hinai, A., Wali, U. K., Rasool, T. A., & Rizvi, S. G. (2017). Experience of intravitreal triamcinolone acetonide for treatment of diabetic macular edema among Omani population. Oman journal of ophthalmology, 10(3), 177.

17. Ozkan, S., Fatih, H., Erkan, C., & Birol, T. (2019). Intravitreal bevacizumab versus bevacizumab and 1 mg triamcinolone acetonide in eyes with bilateral diabetic macular edema. International Eye Science, 19(1), 1-8.
18. Liu, Q., Hu, Y., Yu, H., Yuan, L., Hu, J., Atik, A., ... & Tang, S. (2015). Comparison of intravitreal triamcinolone acetonide versus intravitreal bevacizumab as the primary treatment of clinically significant macular edema. Retina, 35(2), 272-279.