Original Research Paper

Volume - 12 | Issue - 01 | January - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Ophthalomology

ASSESSMENT OF VITREORETINAL INTERFACE ALTERATIONS IN DIABETIC MACULAR EDEMA TREATED WITH INTRAVITREAL ANTI-VEGF INJECTIONS

Dr. Ourfa Ashraf Wani* Senior Resident, Department Of Ophthalmology, SKIMS-MCH, Srinagar, J&K. *Corresponding Author

Dr. Imtiyaz Ahmad Lone Professor, Department Of Ophthalmology, SKIMS-MCH, Srinagar, J&K.

Dr. Waseem Akram Khan Senior Resident, Department Of Medicine, SKIMS, Srinagar, J&K.

ABSTRACT

Background : The introduction of anti-VEGF therapy has had a greater effect on the world of retina than any other advance in the past few decades. This study was conducted to see whether anti-VEGF agents have any kind of fibrotic effect for the development of vitreomacular interface abnormalities, in diabetic eyes without pre-existing fibrotic membranes.

Materials and Methods: This study was a Hospital based retrospective observational study, conducted in the Department of Ophthalmology, SKIMS Medical College Hospital, Srinagar.100 eyes were included in the study. Patients with DME followed at least 9 months were reviewed. Patients were divided into two groups: 50 eyes in anti-VEGF group that had DME and received intravitreal injections and 50 eyes in control group without significant central DME. The groups were comparable in terms of diabetes duration and HbA1c.

Results: A total of 100 eyes were taken in the study that met the inclusion criteria. Vitreomacular interface abnormalities (VMIA) (ERM, VMT and Macular hole) developed in 11 (22%) of the eyes during a follow up period of 36 weeks as compared to 2 eyes (4%) of the control group. This difference is statistically significant ($p = 0.015$). Poor baseline vision was found to be a risk factor for VMIA development.

Conclusion: Our study revealed that patients with clinically significant DME who underwent intravitreal injections had a rate of vitro macular interface abnormalities formation in 22% of eyes during a follow up period of 9 months as compared to 4% eyes of the control group. This difference was statistically significant. VMIA changes in the eyes was associated with initial poor vision. Improvement of BCVA and Central Macular Thickness at the final visit compared with baseline in eyes treated with intravitreal anti-VEGFs was statistically significant.

KEYWORDS : DME, Anti-VEGFs, VMIA.

INTRODUCTION:

Diabetes is a disease of increasing prevalence and in the last few decades it has outnumbered various other epidemics of the world.[1,2] Diabetes mellitus affects 200 million people worldwide.[3] Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years. During the first two decades of disease, nearly all patients with type 1 diabetes and >60% of patients with type 2 diabetes have retinopathy. Vascular endothelial growth factor (VEGF) is overexpressed in diabetic eyes and plays a key role in the development of Diabetic macular edema. VEGF levels are elevated in the vitreous and retina in patients with diabetic retinopathy. VEGF causes a breakdown of the blood-retinal barrier by influencing the tight junctions of retinal endothelial cells and leading to accumulation of fluid in the macula. Therefore, intravitreal VEGF inhibitors are ideal candidates to treat DME by counteracting VEGF overexpression.

The advent of intravitreal anti–vascular endothelial growth factor (anti-VEGF) agents has transformed the treatment of many retinal diseases[4-8] including diabetic macular edema. Three anti-VEGFs are commonly used: aflibercept (Eylea, Regeneron Pharmaceuticals, Tarrytown, NY, USA) and ranibizumab (Lucentis, Genentech, South San Francisco, California, USA) are Food and Drug Administration (FDA) approved treatment for DME, while bevacizumab (Avastin, Genentech, South San Francisco, California, USA) is used off-label.

In recent years, there has been a surge of clinical trials investigating the use of anti-VEGF therapy for DME.[9-11] These trials provide robust evidence that administration of anti-VEGF agents is better than laser therapy both in preserving and in improving vision for patients with DME.

AIM OF THE STUDY:

To see whether anti-VEGF agents have any kind of fibrotic effect for the development of vitreomacular interface abnormalities (VMIA), in diabetic eyes without pre-existing fibrotic membranes.

MATERIALS AND METHODS:

We conducted a hospital based retrospective observational study, in the Department of Ophthalmology, SKIMS Medical College Hospital, Srinagar from 2020 to 2021. 100 eyes were included in the study. Patients with DME followed for at least 9 months were reviewed. Patients were divided into two groups: 50 eyes in anti-VEGF group that had DME and received intravitreal anti-VEGF injections and 50 eyes of the diabetic patients in control group without significant central DME.

The groups were comparable in terms of diabetes duration and HbA1c.

INCLUSION CRITERIA:

Patients with significant DME (≥320 μm) as measured by OCT, with loss of visual acuity.

EXCLUSION CRITERIA:

Pre-existence of any VMIA or other retinal diseases (e.g.ARMD, Vascular occlusions, vasculitis), Glaucoma, Previous treatment for DME eg. prior photocoagulation, any other intraocular surgery. eg. Vitrectomy, Intraocular inflammation, trauma, Iris neovascularization and Media opacities preventing proper imaging.

METHODS:

- Best corrected visual acuity testing.
- Slit lamp biomicroscopy examinaton of the anterior pole before mydriasis to identify cataract, iris neovascularisation;
- Intraocular pressure measurement;
- Gonioscopy to see angle vascularization if any;
- Direct and indirect ophthalmoscopy, including stereoscopic examination of the posterior pole;
- FFA (Fundus fluorescein angiography). Hospital based retrospective observational study.
- OCT for quantitative measurement of macular edema and to detect VMIA changes like epiretinal membrane (ERM) formation, posterior vitreous detachment with vitreomacular traction (VMT) and macular hole formation.

The diagnosis of DME was made by the presence of exudative changes and the thickening of the macular area on the ophthalmoscopic examination and evidence of late macular leakage on FA. Increased CRT, cystic changes, and subretinal fluid might also have been found on the OCT examination. Follow-up measurements of Visual acuity and CMT and detection of VMIA changes were done at week 4,8,12,24 and 36. In patients that required multiple doses of the drugs, repeated intravitreal injections were given at 3 month interval.

RESULTS:

Mean age of cases was 60.2± 9.81 years and that of the control group was 59.8 ± 10.37 years. The difference in the age of the two groups was not statistically significant. The two groups were comparable in terms of age.The male: female ratio of the two groups was also comparable, with p value being statistically in-significant as shown in table 1. In the study group 32% had history of hypertension and 6% had history of CAD. In the control group it was 36% and 10% respectively. P values being 0.673 for hypertension and 0.461 for CAD, thus being statistically insignificant

The mean duration of diabetes in the study group and in the control group was 8.9±3.52 (3-24) years and 8.5±2.59 (4-18) years respectively with a p value of 0.723 which is not statistically significant**.** The HbA1c levels between the two groups were also comparable as shown in table 1.

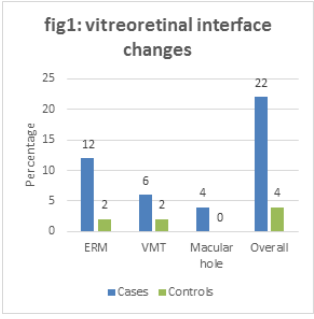
Table 1: demographic characteristics and comorbidities

	cases	controls	p-value
No. of eyes	50	50	
Mean age ± SD (years)	60.2±9.81 (43-80)	59.8±10.37 (41-79)	0.836
Sex Male Female	60% 40%	62% 38%	0.838
Hypertension	32%	36%	
Coronary artery disease	6%	10%	
Duration of Diabetes Mean ±SD (years)	8.9±3.52 (3-24)	8.5±2.59 (4-18)	0.723
Mean HbA1c levels	6.9	7.1	0.368

Vitreoretinal interface changes in two groups:

The resultant fibrotic changes included development of epiretinal membrane, vitreomacular traction and formation of macular hole in 12%, 6% and 4% of cases respectively where as in the control group these changes were seen in 4% of the patients only. P value being 0.015 which is statistically significant as shown in Table 2, fig1.

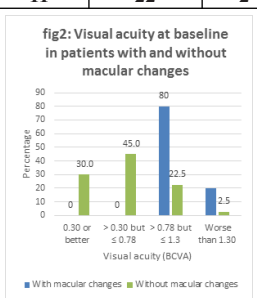
***Statistically Significant Difference (P-value<0.05)**



It was seen that these vitreoretinal interface abnormalities were directly related to the decreased visual acuity at the baseline as depicted in fig2.

Table 2: vitreoretinal interface changes in two groups

Vitreoretinal interface changes	Cases		Controls		P-value
	No.	%	No.	%	
ERM	**6**	**12**	**1**	**2**	**0.015***
VMT	**3**	**6**	**1**	**2**	
Macular hole	**2**	**4**	**0**	**0**	
Total	**11**	**22**	**2**	**4**	



DISCUSSION:

This study was done to assess the development of VMIA in DME patients with intravitreal Anti-VEGFs. Not many studies have been done till date to assess these changes. 100 eyes were taken into study, 50 in the case group and 50 in the control group.

In our study the mean age of cases was 60.2± 9.81 years and that of the control group was 59.8 ± 10.37 years. The difference in the age of the two groups was not statistically significant. The two groups were comparable in terms of age. Out of total 60% cases were males and 40% females in the study group. In the study group 32% had history of hypertension and 6% had history of CAD. In the control group it was 36% and 10% respectively. P values being 0.673 for hypertension and 0.461 for CAD, thus being statistically insignificant. The mean duration of diabetes in the study group and in the control group was 8.9±3.52 (3-24) years and 8.5±2.59 (4-18) years respectively with a p value of 0.723 which is not statistically significant and the mean HbA1c levels of the case group was 6.9 and that of the control group was 7.1. so it can be said that the two groups in our study were comparable demographically and in terms of diabetes duration and HbA1C levels.

Our study revealed that 11 eyes (22%) of a total of 50 eyes who had been submitted the treatment developed VMIA during a follow-up period of 9 months. These changes included development of epiretinal membrane, vitreomacular traction and formation of macular hole in 12%, 6% and 4% of cases respectively where as in the control group these changes were seen in 4% of the patients only. P value being 0.015 which is statistically significant. These changes in the macular interface were seen directly related to the initial decreased visual acuity as can be seen in fig2.

Ebru Nevin Cetin et al[12] conducted a study to assess the macular contraction quantitatively in patients with DME receiving anti VEGF injections and found that the change in distance measurements between the reference points on macular capillary vessels was significant in the study group. During follow-up, the number of cases with ERM changed from 10 to 12 in the study group whereas it remained three in the control group.

In another study conducted by C-K chang et al[13] a total of 201 eyes in 142 patients met the inclusion criteria of the study. VMIA developed in 44 eyes (21.89%) of patients during a mean follow-up period of 40.84 months. The estimated mean incidence of VMIA formation was 6.43% per year. These results were consistent with our study.

CONCLUSION:

The study revealed that patients with clinically significant DME who underwent intravitreal injections of anti-VEGF agents had a higher rate of vitro macular interface abnormalities formation in 22% eyes during a follow-up period of 9 months as compared to eyes of the control group which was only 4%. This difference was statistically significant.

This study also revealed that these VMIA changes in the eyes were associated with initial poor vision.

REFERENCES:

1. A. E. Pontiroli and L. Galli, "Duration of obesity is a risk factor for non-insulin-dependent diabetes mellitus, not for arterial hypertension or for hyperlipidaemia," Acta Diabetologica, vol. 35, no. 3, pp. 130–136, 1998.
2. V. S. Malik, W. C. Willett, and F. B. Hu, "Global obesity: trends, risk factors and policy implications," Nature Reviews Endocrinology, vol. 9, no. 1, pp. 13–27, 2013.
3. International Diabetes Federation. Diabetes atlas 2005. http://www.eatlas.idf.org. Accessed May 2006
4. Solomon SD, Lindsley K, Vedula SS, Krzystolik MG, Hawkins BS. Anti–vascular endothelial growth factor for neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2014;8:CD005139.
5. Virgili G, Parravano M, Menchini F, Evans JR. Anti–vascular endothelial growth factor for diabetic macular oedema. Cochrane Database Syst Rev. 2014;10:CD007419
6. Jampol LM, Bressler NM, Glassman AR. Revolution to a new standard treatment of diabetic macular edema. JAMA. 2014;311(22):2269-2270
7. Braithwaite T, Nanji AA, Lindsley K, Greenberg PB. Anti–vascular endothelial growth factor for macular oedema secondary to central retinal vein occlusion. Cochrane Database Syst Rev. 2014;5:CD007325.
8. Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med. 2011;364(7):603-615.
9. Bandello F, Cunha-Vaz J, Chong NV, et al. New approaches for the treatment of diabetic macular oedema: recommendations by an expert panel. Eye (Lond) 2012;25:485–493
10. Zechmeister-Koss I, Huic M. Vascular endothelial growth factor inhibitors (anti-VEGF) in the management of diabetic macular oedema: a systematic review. Br J Ophthalmol 2012;96:167–178
11. Virgili G, Parravano M, Menchini F, Brunetti M. Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for diabetic macular oedema. Cochrane

Database Syst Rev 2012;12:CD007419
12. Ebru Nevin Cetin , Önder Demirtaş, Nihal Cesur Özbakış & Gökhan Pekel. Quantitative assessment of macular contraction and vitreoretinal interface alterations in diabetic macular edema treated with intravitreal anti-VEGF injections. Graefe's Archive for Clinical and Experimental Ophthalmology 2018;256, 1801–1806.
13. C-K Chang, C-K Cheng & C-H Peng. The incidence and risk factors for the development of vitreomacular interface abnormality in diabetic macular edema treated with intravitreal injection of anti-VEGF. Eye 2017; 31, 762–770.