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EVALUATION OF OUTCOME OF VARIOUS TREATMENT MODALITIES IN PATIENTS WITH DIABETIC MACULAR OEDEMA

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ABSTRACT Introduction: Diabetes mellitus is a disease in which body's ability to produce or respond to the insulin is impaired. Diabetic Retinopathy refers to retinal changes seen in patients with diabetes mellitus. Diabetic maculopathy is when the macula sustains some form of damage leading to visual impairment. Diabetic macular oedema (DME) is the most common cause of vision loss in patients with diabetic retinopathy. This study was done to evaluate the different modes of treatment that can be offered and assessing their outcome over a period of time. **Material and methods :** Our was a prospective observational study which was conducted in the department of the Ophthalmology of tertiary care hospital. Detailed ocular and systemic history was taken. Detailed ocular examination was done including anterior and posterior segment evaluation and investigation. Treatment options included observation, laser therapy, intravitreal injection of anti-VEGF agents or steroids. Post treatment, patients were assessed periodically for a period of 4 months to check the outcome of treatment modality given. **Results :** At baseline, mean BCVA was 0.87 +/- 0.14 (LogMAR chart) and at 1 month follow-up, mean BCVA was improved to 0.57+/- 0.21 (P value <0.00001). Mean CFT was 445.3 +/- 100.5 before intervention and 295.5 +/- 87.8 (P value <0.00001) at one month follow-up. Mean BCVA was found to be 0.86+/- 0.14 and 0.46 +/-0.19 at baseline and 4 months respectively for Ranibizumab injection, 0.85 +/- 0.18 and 0.36 +/- 0.16 at baseline and at 4th month for Bevacizumab injection. **Conclusion :** Both anti - VEGF agents (Ranibizumab and Bevacizumab) showed equivalent improvement in vision and central foveal thickness.

KEYWORDS : diabetic macular edema, ranibizumab, bevacizumab

Introduction:

Diabetes mellitus is a disease in which body's ability to produce or respond to the insulin is impaired resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood. It occurs in two forms: Insulin dependent diabetes mellitus and Non insulin dependent diabetes mellitus. This disease results in generalized macro vascular and micro vascular complications directly affecting kidneys, eyes and peripheral nerves.[1] Diabetic Retinopathy refers to retinal changes seen in patients with diabetes mellitus. It is a micro angiopathy affecting retinal pre-capillary arterioles capillaries and venules. It shows loss of intramural pericytes, thickening of basement membrane and closure of retinal capillaries. The initial loss of pericyte leads to dilatation of blood vessels seen as micro aneurysm and a breakdown of blood vessels allowing leakage of vascular content into surrounding tissues. [2,3]

Occurrence of Diabetic Retinopathy in type 1 diabetes mellitus after 5-10 years was 27% and after 10 years was 71-90%. Occurrence of diabetic retinopathy in type 2 diabetes mellitus was 23% after 11-13 year and after 16 years was 60%. [4]The macula is a crucial part of the retina present at its posterior pole which provides central vision. Diabetic maculopathy is when the macula sustains some form of damage leading to visual impairment. Diabetic macular oedema (DME) is the most common cause of vision loss in patients with diabetic retinopathy.[5]

This study was done to evaluate the occurrence and types of diabetic maculopathy in diabetic patients, their related risk factors, different modes of treatment that can be offered and assessing their outcome over a period of time.

Material and methods:

Our was a prospective observational study which was conducted in the department of the Ophthalmology of tertiary care hospital. Written informed consent was obtained from all patients who participated in the study. This study adhered to the tenets of declaration of Helsinki. The study population consists of 70 patients diagnosed with diabetes mellitus. The study was conducted from August 2019 to September 2021. All diabetic patients more than 18 years of age, giving consent to participate in the study and having diabetic macular oedema were included in the study. Patient suffering from any mental / neurological / debilitating illness and patient having other ocular pathologies which can cause visual impairment were excluded form the study. Detailed history was taken including demographic details, ocular history, duration of DM, treatment taken if any and other systemic diseases. Complete ophthalmological examination was done including visual acuity (best corrected visual acuity), through anterior segment evaluation with slit lam biomicroscopy, tonometry by Goldmann applanation tonometer, fundus evaluation by indirect ophthalmoscopy and with 90D lens slit lam biomicroscopy. Fundus fluorescein angiography was done in appropriate cases. OCT was done in all cases. Blood investigations were done such as complete hemogram, serum creatinine, HbA1c, lipid profile, and other tests depending on individual profile. After diagnosing the type and pattern of diabetic maculopathy on OCT, binocular indirect ophthalmoscope or FFA, intervention was planned. Treatment options included observation, laser therapy, intravitreal injection of anti-VEGF agents or steroids. Post treatment, patients were assessed periodically for a period of 4 months to check the outcome of treatment modality given. Repeat treatment options were given according to response of first treatment modalities.

RESULTS:

In the present study, the mean age of patients with diabetic maculopathy was 55.7 ±10.3 years with range from 34 years to 78 years. Study population consisted of nearly equal gender distribution with 33(52.9%) males & 37(47.1%) females respectively. Mean duration of diabetes mellitus was 12.7 +/- 6.3 years ranging from 6 months to 24 years. Most of the patients were having HbA1C in the range of 8 - 12 signifying poor glycemic control of diabetes mellitus. None of our patients were having HbA1C levels within normal limits. On the first visit, 12(17.14%) Patients had visual acuity between 0.5

to 0.6 on logMAR chart, 15(21.4%) had 0.8 to 0.9, 13(18.5%) had 0.9 to 1 and 30(42.85%) had 1 to 1.10 on logMAR chart.

According to ETDRS classification, 3(4.2%) patients were having mild non proliferative diabetic retinopathy (NPDR), 36(51.42%) patients were having moderate NPDR, 12(17.14%) having severe NPDR and 19(27.14%) were having proliferative diabetic retinopathy(PDR). Out of 70 patients in the study, 33(52.9%) fell under centre involving diabetic maculopathy and remaining 37(47.1%) showed characteristics of non centre involving diabetic maculopathy. Out of 70 patients, 30 (42.85%) received Ranibizumab, 22 (31.42%) received intravitreal TCA, 13 (18.5%) received Bevacizumab and 5(7.14%) received Ozurdex.

At baseline, mean BCVA was 0.87 +/- 0.14 (LogMAR chart), which was re-evaluated after 1 month after giving one dose of intravitreal anti-VEGFs agents (Ranibizumab or Bevacizumab) , triamcinolone (IVTA), steroidal implant (Ozurdex) or one session of laser photocoagulation. At 1 month follow-up, mean BCVA was improved to 0.57+/- 0.21 (P value <0.00001). Mean CFT was 445.3 +/- 100.5 before intervention. At 1 month follow-up, mean CFT decreased to 295.5 +/- 87.8 (P value <0.00001). (Table 1) This suggested that vision is significantly improved after intervention which was simultaneously compared with CFT.

Table 1 - Post 1 month evaluation

Number	Parameter	Baseline value (Mean +/- SD)	After 1 month Value (Mean +/- SD)	P value
1.	Vision	0.87 +/- 0.14	0.57+/- 0.21	< 0.00001
2.	CFT	445.3 +/- 100.5	295.5 +/- 87.8	< 0.00001

Number of intravitreal injections and laser photocoagulation sessions were decided based on patients' response on the 1st month as analysed above. 29(41.42%) patients out of 70 showed desired improvement in vision and CFT and were followed up monthly for routine assessment. Remaining 41(58.57%) patients undergo the same intervention.

26 patients out of 41 showed desired improvement in BCVA after the second dose of intravitreal injection. Mean BCVA before and one month after second dose was 0.67 +/- 0.16 and 0.57 +/- 0.15 (P value < 0.00001). Mean CFT was also evaluated along with, which was 350.6 +/- 70.14 before and 285.8 +/- 66.6 after one month (P value < 0.00001).(Table 2)

Table 2 - Post 2 months evaluation

Number	Parameter	After 1 value (Mean +/- SD)	(Mean +/- SD)	month After 2 month Value		P value
1.	Vision	0.67 +/-	0.16	0.57 +/- 0.15		< 0.00001
2.	CFT	350.6	+/- 70.14	285.8 +/ 66.6		< 0.00001

Remaining 15 patients underwent the same intervention and followed up after a month. Mean BCVA before and after one month of the third dose was 0.59 +/- 0.13 and 0.54 +/- 0.13 (P < 0.0013). Mean CFT was found to be 358.6 +/- 40.6 and 285.9 +/- 45.9 (P value < 0.00001) respectively.(Table 3)

Table 3- Post 3 months evaluation

Number	Parameter	After 2 month Value (Mean +- SD)	After value (Mean +- SD)	3 month	P value
1.	Vision	0.59 +/- 0.13	0.54 +/- 0.13	< 0.0013	
2.	CFT	358.6 +/- 40.6	285.9	+/- 45.9	< 0.00001

In the 4th month, after the commencement of treatment, improvement of vision was statistically assessed using a paired t-test with vision at the time of presentation. Mean BCVA was improved from 0.87 +- 0.14 to 0.47 +/- 0.19 (P value < 0.00001)

Out of 70 patients having diabetic maculopathy, 30 patients were given Ranibizumab and 13 patients were given Bevacizumab. All patients were followed up monthly. After a month of first dose, mean BCVA was improved from 0.86 +/- 0.14 to 0.58 +/- 0.21 in patients who took Ranibizumab injection compared to BCVA improvement from 0.85 +/- 0.18 to 0.48 +/- 0.17 in patients who had Bevacizumab injection. Mean CFT was also evaluated which was 456.5 +/- 109.01 and 294.2 +/-96.7 before and after a month of Ranibizumab injection. Mean CFT was 412 +/-100.9 and 281.1 +/- 84.2 before and after a month of Bevacizumab injection.

All patients were followed up monthly upto 4 months and their baseline BVCA at presentation was compared to 4th month data. Mean BCVA was found to be 0.86+/- 0.14 and 0.46 +/-0.19 respectively for Ranibizumab injection. Mean BCVA was 0.85 +/- 0.18 and 0.36 +/- 0.16 at baseline and at 4th month for Bevacizumab injection. In 5 selected patients of DME, intravitreal dexamethasone implant (Ozurdex) was given at the time of presentation. On monthly followup upto 4 months, patients showed significant reduction in CFT and improvement in visual acuity without repeating the dose.

Discussion:

Ozturk BT et al studied the effects of bevacizumab and ranibizumab on visual function and macular thickness in patients with diabetic macular edema (DME). They found that bevacizumab and ranibizumab are both effective drugs preferred in the treatment of DME. Their comparison of both therapies on the same patients suggested that the effect on BCVA was not statistically different, but ranibizumab provided more decrease in CSMT.[6]

Ford JA et al concluded no difference in effectiveness between ranibizumab and bevacizumab. The number of patients found to have a gain of two or more lines on the ETDRS scale was similar with bevacizumab and with ranibizumab.[7] Schauwvlieghe AM et al compared the effectiveness and costs of 1.25 mg of bevacizumab to 0.5 mg ranibizumab given as monthly intravitreal injections during 6 months in patients with DME and concluded that bevacizumab was not inferior to ranibizumab.[8]

Another study was published by Kurt MM et al about the effects of a single injection of intravitreal ranibizumab or bevacizumab on the retinal vessel size in eyes with diabetic macular edema. The results of this study showed that both injections significantly constricted the retinal blood vessel diameters in DME.[9]

Mello Filho P et al also found similar results concluding that the intravitreal dexamethasone implant is effective and safe for eyes with DME. [10]

Conclusion:

Duration of diabetes mellitus and poor glycemic control are significant risk factor for progression of diabetic retinopathy. Both anti - VEGF agents (Ranibizumab and Bevacizumab) showed equivalent improvement in vision and central foveal thickness. Patients with intravitreal dexamethasone implant showed continuous improvement in CFT found to be long acting. A combined approach of using laser photocoagulation with anti - VEGF agents in selected patients of DME showed significant macular oedema reduction in almost all patients.

REFERENCES

1. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, Chen SJ, Dekker JM, Fletcher A, Grauslund J, Haffner S. Global prevalence and major risk factors of diabetic retinopathy. Diabetes care. 2012 Mar 1;35(3):556-64.
2. Antonelli-Orlidge A, Smith SR, D'Amore PA: Influence of pericytes on capillary endothelial cell growth. Am Rev Respir Dis 140:1129–1131, 1989
3. Ademis AP, Miller JW, Bernal MT, et al. Increased vascular endothelial growth factors in the vitreous of eyes with proliferative diabetic retinopathy. Am J Ophthalmology ,Am J Ophthalmology, 1994; 118:445-50.
4. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, Chen SJ, Dekker JM, Fletcher A, Grauslund J, Haffner S. Global prevalence and major risk factors of diabetic retinopathy. Diabetes care. 2012 Mar 1;35(3):556-64.
5. Lee CS, Lee AY, Sim DA, et al. Re-evaluating the definition of intra retinal micro vascular abnormalities and neovascularization elsewhere in diabetic retinopathy using optical coherence tomography and fluorescein angiography. AM J Ophthalmol. 2015;159(1):101-10.e1l.
6. Ozturk BT, Kerimoglu H, Bozkurt B, Okudan S. Comparison of intravitreal bevacizumab and ranibizumab treatment for diabetic macular edema. Journal of Ocular Pharmacology and Therapeutics. 2011 Aug 1;27(4):373-7.
7. Ford JA, Elders A, Shyangdan D, Royle P, Waugh N. The relative clinical effectiveness of ranibizumab and bevacizumab in diabetic macular oedema: an indirect comparison in a systematic review. Bmj. 2012 Aug 13;345.
8. Schauwvlieghe AM, Dijkman G, Hooymans JM, Verbraak FD, Hoyng CB, Dijkgraaf MG, Van Leeuwen R, Vingerling JR, Moll AC, Schlingemann RO. Comparing the effectiveness and costs ofbevacizumab to ranibizumab in patients with diabetic macular edema: a randomized clinical trial (the BRDME study). BMC ophthalmology. 2015 Dec;15(1):1-6.
9. Kurt MM, Çekiç O, Akpolat Ç, Elcioglu M. Effects of intravitreal ranibizumab and bevacizumab on the retinal vessel size in diabetic macular edema. Retina. 2018 Jun 1;38(6):1120-6.

10. Mello Filho P, Andrade G, Maia A, Maia M, Neto LB, Neto AM, Brasil OM, Minelli E, Dalloul C, Iglicki M. Effectiveness and safety of intravitreal dexamethasone implant (Ozurdex) in patients with diabetic macular edema: a real-world experience. Ophthalmologica. 2019;241(1):9-16.