Original Article

Importance of Combination of Intravitreal Bevacizumab and Panretinal Photocoagulation in Proliferative Diabetic Retinopathy

Nidhi Priyadarshini, Preeti Gupta, Chander M. Kohli*

Department of Ophthalmology, Hind Institute of Medical Sciences, Sitapur, Uttar Pradesh, India.

Abstract

Introduction: Diabetic retinopathy is a vascular condition of the retina that develops due to diabetes mellitus (DM). This study aimed to compare intravitreal bevacizumab, pan-retinal photocoagulation or a combination of both in proliferative diabetic retinopathy.

Method: In this prospective, randomized interventional study, 180 patients with PDR were enrolled and divided into three equal groups, i.e., Group A patients treated with laser alone and group B- patients treated with anti-VEGF alone and Group C- patients treated with anti-VEGF and laser. The patient's detailed history and clinical and demographical data were recorded and compared. The examination was done, including visual acuity assessment with Snellen's chart, slit-lamp biomicroscopic examination, Intraocular pressure and pupillary assessment for optic nerve dysfunction.

Results: The mean age of group-A, B and C were 57.13 ± 6.88, 55.62 ± 5.97 and 54.86 ± 4.98 were comparable. At the same time, most of the patients were between the age group of 58–66 years [25(41.67%)]. Majority of the patients were male in all three groups. A significant difference was observed in mean FBS and duration of diabetes. In group A and C, most patients affected eye was left [35(58.33%)] and [34(56.67)], respectively, while in group B right eye was affected [33(55.00%)]. The mean VA Log MAR was found to be significant among the three groups. Mean SNELLENS and IOP were insignificant among the groups. At first, follow up the mean VA LOG MAR, SNELLENS, FFA and OCT were found to significant among the groups. At second follow-up, the mean VA LOG MAR was significant. Intragroup analysis between the treatment of the eye was found insignificant, while the rest of the parameters and characteristics were found significant.

Conclusion: The present study suggests that the anti-VEGF + PRP were the best treatment regime, followed by anti-VEGF, and PRP was the least effective.

Keywords: Diabetes mellitus, Diabetic retinopathy, Proliferative diabetic retinopathy, Diabetic macular edema, Retinal ischemia, Pan retinal photocoagulation, Vascular endothelial growth factor.

Introduction

Diabetes Mellitus is a chronic, metabolic multisystem illness that affects the world's working-age population.[1] According to the WHO, 31.7 million individuals in India had diabetes mellitus (DM) in 2000. This statistic is expected to climb to 79.4 million by 2030, the most of any country on Earth. Approximately two-thirds of Type 2 diabetics and nearly all Type 1 diabetics are likely to develop diabetic retinopathy (DR) over time.[2] Diabetic retinopathy, a vascular condition of the retina that develops as a result of diabetes mellitus, is the largest cause of blindness in the United States, frequently affecting working-age individuals. It is defined by evidence of retinal ischemia (microaneurysms, hemorrhages, cottonwool spots, intraretinal microvascular anomalies, aberrant venous calibres, and neovascularization) and/or increased retinal vascular permeability. A variety of factors can cause vision loss, including neovascularization, which can result in

Address for correspondence: Chander M. Kohli,
Department of Ophthalmology, Hind Institute of Medical Sciences, Sitapur, Uttar Pradesh, India.
E-mail: nidhitiwary25@gmail.com

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vitreous hemorrhage and/or retinal detachment, macular edema, and retinal capillary nonperfusion.[3] Although retinopathy occurs in the majority of people with long-standing diabetes, its incidence can be decreased with aggressive control of hyperglycemia and hypertension.[4,5] Because retinopathy frequently goes unrecognized until vision loss occurs, early detection, prompt treatment, and proper care can help prevent or delay vision loss. Diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR) are two major DR complications responsible for visual morbidity. The method by which DME and PDR develop is due to increased VEGF levels caused by ischemia and hypoxia resulting from diabetic microvascular alterations. For the last few decades, the diabetic retinopathy treatment study (DRS) and early treatment diabetic retinopathy study (ETDRS) have established that the cornerstone of treatment for PDR is laser photocoagulation. According to early treatment diabetic retinopathy, immediate focal laser photocoagulation treatment reduces vision loss due to macular odema by 50%. In PDR, laser photocoagulation was initially performed using the blue-green argon laser.[1,6-8] Over the last decade, intravitreal anti-VEGF medicines have revolutionized the therapy of diabetic eye disease. Bevacizumabis a humanized monoclonal antibody that inhibits all VEGF-A isoforms competitively. Alternatively, laser PRP is more durable. These medicines work by inhibiting various kinds of endogenous VEGF, although the duration of impact is brief, necessitating repeated intravitreal injections.[9,10] The purpose of this study was to compare PRP with intravital injections in order to determine which is more comfortable and results in less retinal functional loss.

Material and Methods

The present study was carried out in the Department of Ophthalmology, HIMS, Sitapur. This prospective randomized interventional study was conducted from 2021 to 2022. The patients with PDR with and without center involving macular edema- vision more than or equal to 6/12 or edema less than 300 micron on OCT were enrolled as per the inclusionand exclusion criteria (Laser not possible due to significant media opacity, Pregnant, lactating or women planning family within a year. Recent ocular surgery, vision very poor in both eyes which might require early vitrectomy, H/O of prior treatment for retinopathy (anti VEGF or PRP), patients with glaucoma). After taking valid informed consent, patients were divided into three groups of 60 each. All the patients were evaluated with history and thoroughexaminationincludingvisual acuity assessment with Snellen's chart, Slit-lamp biomicroscopic examination (HUVITZ-HS- 5000(X3)(HKG)) of anterior segment including examination of iris to look for NVI, Intraocular pressure (IOP) was measured by applanation tonometer (APPASAMY REF AATM-5001) and pupillary assessment for optic nerve dysfunction was done. Gonioscopy (ZEISS 4 MIRROR) was done before dilation. Clinical examinations such as CBC, FBS, PPBS, viral marker(HBsAg, HCV, HIV), COVID Ag test, FLP were recorded and compared. Ocular investigation was done using Humphrey Field Analyser (IRC medical equipment IVS- 2018). Fundus fluorescein angiography and optical coherence tomography were also done. Diabetic retinopathy was graded according to the international clinical diabetic retinopathy severity scale. All the patients were followed up to 12 and 24 weeks. Slit lamp-based Laser delivery system was used [Frequency Double Nd:YAG (532nm)] in the PRP procedure. Oral antibiotic was given for 5 days and topical antibiotic drops for 1 week.

Statistical Analysis

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA) for Windows program (21.0 version). The continuous variables were evaluated by mean (standard deviation) or range value when required. The dichotomous variables were presented in number/frequency. Analysis by ANOVA (one way) with 95% confidence interval was used to compare the means between the groups. A *p-value* of < 0.05 or 0.001 was regarded as significant.

Results

The mean age of group-A, B and C were 57.13 ± 6.88, 55.62 ± 5.97 and 54.86 ± 4.98. In all three groups, most patients were observed in the age distribution of 58-66 years with a non-significant difference of [P=0.7108]. The maximum number of patients were males.[Table 1]The mean FBS of enrolled patients in Group-A, B and C were 164.17 ± 61.21, 228.50 ± 82.16 and 169.92 ± 46.45, respectively. The mean PPBS of enrolled patients in Group-A, B and C were 234.60 ± 55.38, 314.67 ± 94.04 and 245.93 ± 67.43, respectively. Overall, a significant difference was observed [P<0.0001*] in FBS and PPBS among the groups. Mean Hb, HbA1c, HDL, Triglycerides, duration of diabetes, and treatment of disease was observed and found insignificant. [Table 2] In group-A, most patients affected eye was left [35(58.33%)] followed by the right eye [25(41.67%)]. However, in group-B, most patients affected eye was right [33(55.00%)] followed by left [27(45.00%)]. Furthermore, in group-C, most patients left eye [34(56.67)] was affected, followed by right eye [26(43.33%)]. Overall, a non-significant [p=0.2802] association was observed in the affected eye among the groups.[Table 1] The mean VA Log MAR was found significant [Table 2], whereas the mean SNELLEN was found non-significant. In most of the patients, the duration of diabetes was 2 years in all three groups. [Table 1] The mean IOP, AS, OCT were also found

Table 1: Demographical and clinical data of enrolled patients.

		Group-a		*Group-b*		*Group-c*		*P-value*
		N	*%*	*N*	*%*	*N*	*%*	
Age	31-39	1	1.67	1	1.67	2	3.33	X=14.68 P=0.0657
	40-48	9	15.00	6	10.00	8	13.33	
	49-57	21	35.00	36	60.00	21	35.00	
	58-66	25	41.67	12	20.00	19	31.67	
	67-75	4	6.67	5	8.33	10	16.67	
	Mean ± sd	57.13	6.88	55.62	5.97	54.86	4.98	F=2.230 p=0.1106
Gender	Male	35	58.33	32	53.33	30	50.00	X=0.8496 p=0.6539
	Female	25	41.67	28	46.67	30	50.00	
Treatment of disease	Insulin	20	33.33	24	40.00	21	35.00	X=0.6261 p=0.7312
	Ohd	40	66.67	36	60.00	39	65.00	
Affected eye	Righteye	25	41.67	33	55.00	26	43.33	X=2.545 p=0.2802
	Left eye	35	58.33	27	45.00	34	56.67	
Snellen	6/12	37	61.67	46	76.67	43	71.67	X=3.333 p=0.1889
	6/9	23	38.33	14	23.33	17	28.33	
Duration (Years)	1	16	26.67	18	30.00	8	13.33	X=9.47 p=0.0504
	2	29	48.33	34	56.67	32	53.33	
	3	15	25.00	8	13.33	20	33.33	
As	Nvi-	29	48.33	40	66.67	36	60.00	X=4.251 p=0.1193
	Nvi+	31	51.67	20	33.33	24	40.00	
Ffa	Focal	22	36.67	12	20.00	1	1.67	X=30.97 p<0.0001*
	Diffuse	31	51.67	25	41.67	40	66.67	
	Mixed	7	11.67	23	38.33	19	31.67	
Diagnosis	1	30	50.00	30	50.00	30	50.00	X=0 p>0.9999
	2	30	50.00	30	50.00	30	50.00	

Diagnosis of othereye	Pdr	38	63.33	33	55.00	33	55.00	X=1.139 P=0.5659
	Pdr+me<300	22	36.67	27	45.00	27	45.00	

Table 2: Baseline characteristics of enrolled patients

	GROUP-A		*GROUP-B*		*GROUP-C*		*P-value*
	MEAN	*SD*	*MEAN*	*SD*	*MEAN*	*SD*	
FBS (mg/dl)	164.17	61.21	228.50	82.16	169.92	46.45	F=18 P<0.0001*
PPBS (mg/dl)	234.60	55.38	314.67	94.04	245.93	67.43	F=20.53 P<0.0001*
Hb (mg/dl)	10.52	1.74	10.75	1.83	10.79	1.77	F=0.4019 P=0.6696
HbA1c	8.28	1.21	8.63	2.89	8.93	1.36	F=1.633 P=0.1983
HDL (mg/dl)	37.45	9.37	37.00	10.45	35.97	11.04	F=0.3249 P=0.7230
TRIGLYCERIDE mg/dl	215.42	14.19	214.35	13.72	215.30	14.85	F=0.1014 P=0.9036
Durationofdiabetes (Years.)	5.43	1.66	4.15	1.24	6.20	2.01	F=23.16 P<0.0001 *
TREATMENT OF DISEASE	1.67	0.47	1.60	0.49	1.65	0.48	F=0.3384 P=0.7133
VA Log MAR	0.26	0.05	0.28	0.04	0.27	0.04	F=3.158 P=0.0449*
Intraocular Pressure (IOP) Mmhg	15.95	2.24	16.45	2.62	16.55	2.79	F=0.9458 P=0.3903
OCT Um	267.95	19.98	267.9	20.43	269.13	21.56	F=0.0680 8 P=0.9342

Table 3: Va log mar, oct and diagnosis at first follow-up of enrolled patients (12 weeks)

	Group-a		Group-b		Group-c		P-value
	Mean	Sd	Mean	Sd	Mean	Sd	
Va log mar	0.25	0.05	0.23	0.05	0.26	0.05	F=5.6 p=0.0044*
Oct	265.48	15.82	279.17	24.09	272.83	18.03	F=7.311 p=0.0009*
Diagnosis	2.15	0.85	2.27	0.86	2.08	0.80	F=0.7906 p=0.4552

Table 4: VA Log MAR, OCT and Diagnosis at second follow-up of enrolled patients (24 weeks)

	Group-a		Group-b		Group-c		P-value
	Mean	Sd	Mean	Sd	Mean	Sd	
Va Logmar	0.23	0.06	0.22	0.06	0.25	0.05	F=4.33 p=0.0146*
Oct	272.33	23.12	274.45	23.49	278.85	22.58	F=1.238 p=0.2925

to have a non-significant difference.[Table 2] At the first follow up (12weeks) the mean VA Log MAR, SNELLENS, FFA, OCT were observed and found significant among all the groups. While analyzing DIAGNOSIS of enrolled patients in Group-A, B and C at follow-up 1. The mean DIAGNOSIS in Group-A, B and C were 2.15 ± 0.85, 2.27 ± 0.86 and 2.08 ± 0.80 are comparable. Furthermore, a non-significant difference was observed [P=0.4552]. [Table 3; Figure-1 and 2] At the second follow up (24 weeks) the mean VA LOG MAR in Group-A, B and C were 0.23 ± 0.06, 0.22 ± 0.06and 0.25 ± 0.05. Group-C showed the highest mean VA LOG MAR. In group-A, most of the patients were STABLE [36(60.00%)] followed by PDR+ME [13(21.67%)]. Similarly, in group-B majority of the patients were STABLE [37(61.67%)] followed by PDR+ME [17(28.33%)]. Furthermore, in group-C 28 patients were diagnosed with PDR+ME [28(46.67%)] and 28 were STABLE [28(46.67%)]. Overall, a significant difference was observed. [Table 4; Figures 3-5] Intra group analysis was done with respect to age, gender and other baseline characteristics except for the treatment of the eye as per OCT, every other characteristic and parameter showed a significant difference among groups. Intra group analysis at 12 and 24 weeks were done and there was also observed statistically a significant difference.

Discussion

a chronic, metabolic multisystem illness affecting the world's working-age population, diabetes mellitus is characterized by high blood glucose levels and impaired insulin production.[1] With a population of 1.2 billion people, India is on track to

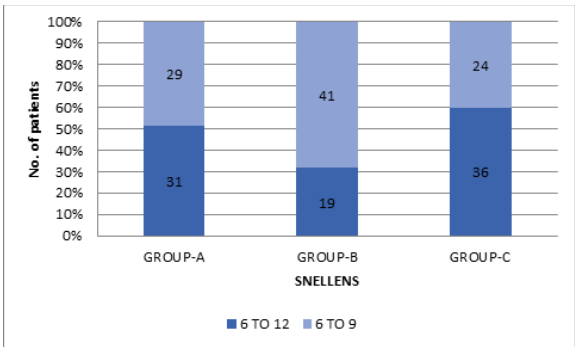

Figure 1: SNELLENS of enrolled patients in Group-A, B and C at first follow-up (12 weeks)

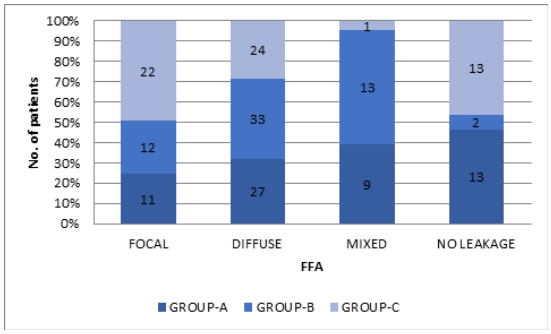

Figure 2: FFA of enrolled patients in Group-A, B and Cat first follow-up (12 weeks).

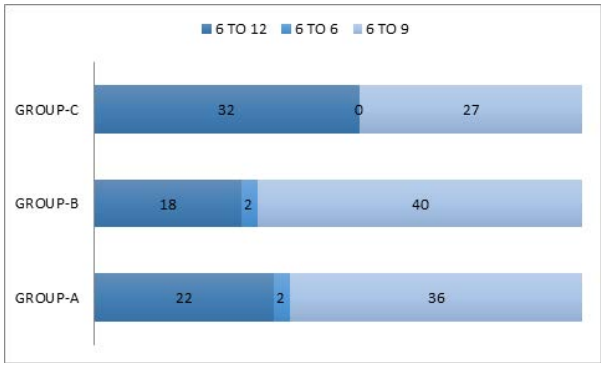

Figure 3: SNELLENS of enrolled patients in Group-A, B and C at second follow-up (24 weeks).

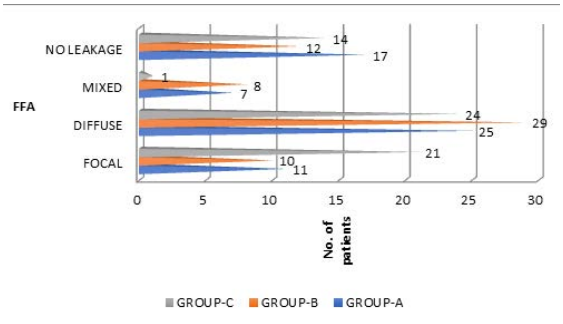

Figure 4: FFA of enrolled patients in Group-A, B and C at second follow-up (24 weeks).

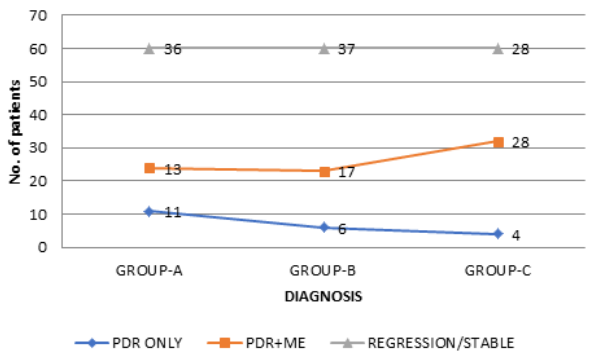

Figure 5: Diagnosis of enrolled patients in Group-A, B and C at second follow-up (24 weeks).

become the world's diabetes capital. Diabetes mellitus (DM) was diagnosed in 31.7 million people in India in 2000, according to the World Health Organization. 79.4 million people are expected to be living in this country by 2030, making it the most populous country on the planet. About two-thirds of Type 2 diabetics and nearly all Type 1 diabetic are at risk for developing diabetic retinopathy (DR) over the course of their lives.[2] Diabetes Mellitus (DM) is a hyperglycemic clinical condition. It is a prevalent condition that manifests itself in one of two ways: Type 1 (formerly known as IDDM) or Type 2. (Previously known as NIDDM). This condition is associated with a variety of macro and microvascular consequences.In the current study,a total of 180 cases were enrolled that further underwent different treatment regimes, i.e., Anti VEGF (Group-A), PRP (Group-C) and Anti VEGF + PRP both (Group-B). However, Jorge, D.M *et al.*,[11] included 73 cases, Rebbeca *et al.*,[12] included 76 eyes in their research. Darabe, F *et al.*,[13] enrolled 90 patients for their investigation. He, F *et al.*,[14] enrolled 44, Choi W *et al.*,[15] enrolled 93 and Obeid A *et al.*,[16] enrolled 76 eyes for their study. In current study while analyzing the age of the included patients, we found that the age of patients enrolled in the study ranged between 22-75 years, with the mean age of 57.13 ± 6.88 for group-A, 55.62 ± 5.97 for Group B and 49.87 ± 15.88 for Group-C. Also, the statistically significant difference among them was observed with p<0.0001*. However, in the study performed by Jorge, D.M *et al.*,[11] broad area of working age group was considered. Whereas in the study performed by Rebbeca *et al.*,[12] the patients of 18-65 years age group were enrolled. Similarly, in the study by Darabe, F *et al.*,[13] all patients aged ≥18 year who presented with first-time PDR with almost the same changes in both eyes with no prior retinal laser besides macular laser treatment were included. Further, in the investigation of He, F *et al.*,[14] no age was considered as a prominent isolative factor. However, in the study by Choi W *et al.*,[15] the mean age of participants was 58.7. Lastly, in the study of Obeid A *et al.*,[16] the mean age of enrolled cases was 54.10 ± 12.8.In the current study, while analyzing the gender of the enrolled patients, we found that, the majority of the patients were male in all three group-A [35(58.33%)], B [32(53.33%)] and C [30(50.00%)] followed by females in all three group-A [25(41.67%)], B [28(46.67%)] and [30(50.00%)]. There is a non-significant difference was observed [p=0.6539] between gender and all three groups. However, in the study performed by Jorge, D.M *et al.*,[11]the male:female ratio in group A was 15:20, and 18:17 in group B, respectively. Whereas in the study performed by Rebbeca *et al.*,[12] the male (%) and female (%) in group-A was 58.25 and 41.75, respectively while 62.96 and 37.04 in group B respectively. Further, in the investigation of Darabe, F *et al.*,[13] He, F *et al.*,[14] and Choi W *et al.*,[15] no gender was considered as a prominent isolative factor. Lastly, in the study of Obeid A *et al.*,[16] the observed male: female ratio was 31:28. Inthe present study, we have also recorded and analyzed the associative clinical features of the enrolled included patients. The mean FBS of enrolled patients in group A, B and C were 164.17 ± 61.21, 228.50 ± 82.16 and 169.92 ± 46.45, along with the significant difference. A significant difference was observed between mean PPBS and groups A, B and C. The mean Hb in group A, B and C were 10.52 ± 1.74, 10.75 ± 1.83 and 10.79 ± 1.77 are comparable. However, the mean HbA1c in group A, B and C were comparable. Similarly, mean HDL and triglycerides in group-A, B and C were comparable. Similarly, the mean duration of diabetes was maximum in group- C[6.20 ± 2.01] followed by group A[5.43 ± 1.66] and the least mean duration of diabetes in group B[4.15 ± 1.24]. Further, in the same series, the mean treatment of disease was also comparable and an insignificant difference was observed. While treatments most of the patients were treated by OHD [40(66.67%), 36(60.00%) and 39(65.00%)] in group-A, B and C followed by insulin [20(33.33%), 24(40.00%) and 21(35.00%)]. The mean VA Log MAR in group A, Band C were 0.26 ± 0.05, 0.28 ± 0.04and 0.27 ± 0.04 are comparable. The mean duration of diabetes was maximum in group C [6.20 ± 2.01] with a significant difference among them [p<0.0001*]. The mean VA Log MAR in group A, B and C were 0.26 ± 0.05, 0.28 ± 0.04 and 0.27 ± 0.04 are comparable. Also, a significant difference was observed [p=0.0449*] between mean VA Log MAR and group A, B and C of enrolled patients.While analyzing in group A, most of the patients showed 6/12 SNELLEN [37(61.67%)] followed by 6/9[23(38.33%)]. In group B, most of the patients showed 6/12 SNELLEN [46(76.67%)] followed by 6/9[14(23.33%)]. Similarly, in group C, most of the patients showed 6/12 SNELLEN [43(71.67%)] followed by 6/9[17(28.33%)]. While analyzing, most of the patients in Group-A had a duration of symptoms over 2 yr. [29(48.33%)] followed by 1 yr. [16(26.67%)]. However, in group B, most of the patients had a duration of symptoms over 2yr. [34(56.67%)] followed by 1yr. [18(30.00%]. Furthermore, in group C, majority of the patients had a duration of symptoms over 2 year. [32(53.33%)] followed by 3 yr. [20(33.33%)]. The mean intraocular pressure

(IOP) in group A, B and C were 15.95 ± 2.24, 16.45 ± 2.62and 16.55 ± 2.79. In group A, most of the patients fell in NVI+ [31(51.67%)] than NVI- [29(48.33%)]. However, in group B majority of the patients fell in NVI- [40(66.67%)] than NVI+[20(33.33%)]. Further, in group C most patients fell in NVI- [36(60.00%)] than NVI+[24(40.00%)]. The mean OCT in group A, B and C were 267.95 ± 19.98, 267.9 ± 20.43 and 269.13 ± 21.56 are comparable. In group A, most of the patients fell in DIFFUSE FFA [31(51.67%)] followed by FOCAL FFA [22(36.67%)]. However, in group B majority of the patients showed in DIFFUSE FFA [25(41.67%)] followed by MIXED FFA [23(28.33%)]. In group-A, most of the patients were diagnosed with proliferative diabetic retinopathy (PDR) [38(63.33%)] followed by PDR+ME<300 [22(36.67%)]. However, in group B majority of the patients diagnosed with proliferative diabetic retinopathy (PDR) [33(55.00%)] followed by PDR+ME<300 [27(45.00%)]. A significant difference was observed [p<0.0001*] in intragroup analysis between groups A, B and C and FBS. Intragroup analysis in group A and PPBS showed that group A1(OCT<250) [254.10 ± 71.52] had higher mean PPBS than group A2(OCT>250-300) [215.10 ± 16.07]. However, in intragroup analysis in group B and PPBS showed that Group-B1(OCT<250) [296.00 ± 79.61] had lower mean PPBS than group B2(OCT>250-300) [333.33 ± 103.22]. Similarly, intragroup analysis in group C and PPBS showed that group-C1(OCT<250) [222.8 ± 64.8] had lower mean PPBS than group-C2(OCT>250-300) [269.10 ± 61.82]. Overall, a significant difference was observed [p<0.0001*] in intragroup analysis between group A, B and C and PPBS. Intragroup analysis in group A and Hb showed that group- A1(OCT<250) [11.4 ± 1.58] had higher mean Hb than group-A2(OCT>250-300) [9.63 ± 1.43]. However, in intragroup analysis in group B and Hb showed that group-B1(OCT<250) [12.03 ± 1.27] had higher mean Hb than group- B2(OCT>250-300) [9.47 ± 1.33]. Similarly, Intragroup analysis in group C and Hb showed that group-C1(OCT<250) [11.95 ± 1.21] had higher mean Hb than group-C2(OCT>250-300) [9.63 ± 1.45].Overall, a significant difference was observed in intragroup analysis between group-A, B and C and Hb1Ac.Intragroup analysis in group A and HDL showed a significant difference [P<0.0001*]. Intragroup analysis in groups and the treatment of disease showed a significant difference. Intragroup analysis in group A and DOD showed that group-C1(OCT<250) [6.9 ± 2.15] had higher mean DOD.Intragroup analysis on duration of symptoms showed that in group-A1(OCT<250) most of the patients had a duration of symptoms over 2 years [15(50.00%)] followed by 1 year. [15(40.00%)]. However, in group A2(OCT>250-300) most of the patients had duration of symptoms over 2 years [14(46.67%)] followed by 3 years. [13(43.33%)]. However, in intragroup analysis in group B and duration of symptoms showed that in group B1(OCT<250) most of the patients had duration of symptoms over 2 years [14(46.67%)] followed by 1 yr. [13(43.33%)]. However, in group-B2(OCT>250-300) most of the patients had duration of symptoms over 2years [20(66.67%)] followed by 3 and 1 yr. [5(16.67%)]. However, in intragroup analysis in Group C and Duration of symptoms showed that in Group-C1(OCT<250) most of the patients had a duration of symptoms over 2years [16(53.33%)] followed by 3 yr. [12(40.00%)]. However, in Group-C2(OCT>250-300) most of the patients had duration of symptoms over 3 years [14(46.67%)] followed by 2 years. [11(36.67%)]. A significant difference was observed in intragroup analysis between group A, B and C and VA log MAR. Intragroup analysis in group A and SNELLENS showed that in group A1(OCT<250) most of the patients had 6/12 SNELLENS [17(56.67%)] followed by 6/9 [13(43.33%)]. However, in group A2(OCT>250-300) most of the patients had 6/12 SNELLENS [20(66.67%)] followed by 6/9 [10(33.33%)]. However, in intragroup analysis in group B and SNELLENS showed that in group B1(OCT<250) most of the patients had 6/12 SNELLENS [27(90.00%)] followed by 6/9 [3(10.00%)]. However, in group B2(OCT>250–300) most of the patients had 6/12 SNELLENS [19(63.33%)] followed by 6/9 [11(36.67%)]. However, in intragroup analysis in group C and SNELLENS showed that in group C1(OCT<250) most of the patients had 6/12 SNELLENS [26(86.67%)] followed by 6/9 [4(13.33%)]. However, in group-C2(OCT>250-300) most of the patients had 6/12 SNELLENS [17(56.67%)] followed by 6/9 [13(43.33%)]. A significant difference was observed [p<0.0001*] in intragroup analysis between group A, B and C and IOP. Intragroup analysis in group A and AS showed that group-A1(OCT<250) [1.53 ± 0.50] and group-A2(OCT>250–300) [1.50 ± 0.50] were comparable. Intragroup analysis in group A and OCT showed that group A1(OCT<250) [248.53 ± 2.80] had lower mean OCT than group A2(OCT>250–300) [287.37 ± 6.04]. However, in intragroup analysis in group B and OCT showed that group- B1(OCT<250) [248.00 ± 3.56] had higher mean OCT than group B2(OCT>250–300) [287.80 ± 5.52]. Likewise, intragroup analysis in group C and OCT showed that group- C1(OCT<250) [247.93 ± 3.72] had lower mean OCT than group C2(OCT>250–300) [290.33 ± 4.15]. A significant difference was observed [p<0.0001*] in intragroup analysis between groups A, B and C and OCT. Intragroup analysis in group A and FFA showed a significant difference [p<0.0001*] in intragroup analysis between group A, B and C and FFA.In the study performed by Jorge, D.M *et al.*,[11] the explained that, PPV with preoperative IVB is associated with more rapid clearance of VH and improvement in BCVA than IVB injections alone. However, after 24 weeks of follow-up, the reduction in VH score and BCVA were similar between both treatment strategies. Whereas in the study performed by Rebbeca *et al.*,[12] they observed that, according to the improvement in results of BCVA and timing of regression of neovessels status after combined intravitreal bevacizumab injection and PRP demonstrated that intravitreal bevacizumab is a beneficial adjunctive treatment for high-risk PDR. Though

multiple reinjections are required to maintain a visual improvement some patients have regression of retinal neovessels. Similar to our study, Darabe, F *et al.*,[13]concluded that IVB is a safe and effective adjunctive treatment to PRP in the short term. PRP plus IVB is associated with a higher and early rate of regression of active NVs than PRP alone in patients with PDR. PRP plus IVB treated eyes also showed better visual outcomess than PRP only eyes in PDR. Further studies will be needed to determine whether IVB plus PRP is a satisfactory treatment for the prevention of vision-threatening complications such as vitreous hemorrhage and tractional retinal detachment. However, He, F *et al.*,[14] concluded that in their study the combination of intravitreal conbercept injection with PRP resulted in a higher reduction rate of NVE than PRP alone in PDR patients. OCTA has an important role in visualizing the NVE area and monitoring its response to therapies. Finally, larger studies with longer follow- up are required to ascertain our preliminary findings. Further, in their study Choi W *et al.*,[15] suggested that IVB injection before PRP leads to decreased CMT in comparison to CMT in patients with PRP alone. These findings suggest that IVB injection prior to PRP may be an effective adjunctive modality for preventing ME after PRP or treating existing ME in patients with PDR. These findings are relevant to ours. In their research Obeid A *et al.*,[16] observed significant differences in anatomic outcomes of PDR eyes that are LTFU after receiving IVIs with anti-VEGF agents compared with eyes undergoing PRP. Moreover, their results suggested that there also may be a significant difference in functional outcomes, although this will remain difficult to interpret given the lack of randomization between the 2 groups. Although both treatment methods are effective for PDR, physicians need to take into consideration the potential differential outcomes associated with inconsistent follow-up when selecting the type of treatment.

Conclusion

The primary goal of the present study was to compare intravitreal bevacizumab, panretinal photocoagulation or a combination of both in proliferative diabetic retinopathy. Based on the findings of this study, we can extrapolate that, the results of the present study post-follow-up suggested that, ant-VEGF + PRP were the best as treatment regime, followed by anti-VEGF and then after least effective one was PRP. However, to bypass the confounding variables and increase the present research's efficacy, we recommend a strong, multicentric study with a high descriptive sample size.

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