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Adjunctive Preoperative Ranibizumab (Luecentis) Before Vitrectomy for Vitreous Haemorrhage in Diabetics

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ABSTRACT

Background: When proliferative diabetic retinopathy is treated with pars plana vitrectomy, post-operative vitreous bleeding is prevalent. Complications such as these impede visual rehabilitation and may demand additional surgical treatments.
Aim of The Work: Comparison of CCT measurements using specular microscope, pentacam and anterior segment OCT in individuals with healthy corneas.
Patients and Methods: More than one month of persistent diabetic vitreous bleeding was included in this randomized, prospective research. There were two groups of eyes that were considered eligible: Twenty eyes in Group A had no intravitreal injections, while twenty eyes in Group B received a ranibizumab intraoperative intravitreal injection.
Results: PDR problems are related with considerable improvement in postoperative BCVA in one week, one month, and three months postoperatively in both group A and group B compared to preoperative BCVA. Postoperative BCVA at 3 months which was 0.953± 0.451 and A statistically significant difference (p = 0.000) was found between the two groups.
Conclusion: In patients who got preoperative intravitreal ranibizumab injection, the incidence of postoperative vitreous hemorrhage is lower than in individuals who did not receive IVR injection. There was no statistical significance despite this association, however this is because there were only a few cases in this study.

Keywords: *Vitrectomy ; Vitreous Haemorrhage ; Diabetics.*

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INTRODUCTION

When proliferative diabetic retinopathy is treated with pars plana vitrectomy, post-operative vitreous bleeding is prevalent. Complications such as these impede visual rehabilitation and may demand additional surgical treatments [(1)].

(Ranibizumab) An antibody that binds and inhibits both isoforms of VEGF-A (Lucentis® by Genentech, Inc., South San Francisco, CA) has been shown to cause regression of retinal neovascularization in patients with PDR who are taking ranibizumab. An increasing number of studies have shown that intravitreal Ranibizumab can be used before plana vitrectomy to prevent postoperative VH. [1]

PATIENTS AND METHODS

Persistent vitreous hemorrhage in patients with diabetes for more than a month is the focus of this prospective trial, which includes 40 eyes.

Two groups of patients were formed:

Group (A): (control group): 20 eyes underwent pars plana vitrectomy and left on air without injection of Ranibizumab.

Group (B): 20 eyes underwent pars plana vitrectomy and left on air with preoperative injection of Ranibizumab

All surgical procedures and follow up were carried out at Al-Azhar university hospitals.

Before any surgical procedure was performed, all patients had given their informed consent. Patients were informed of the treatment's dangers, advantages, alternatives, and limits.

Inclusion criteria:

More than a month of continuous diabetic vitreous hemorrhage.

Exclusion criteria:

Retinal detachment (Tractional or Rhegmatogenous) or advanced fibrovascular proliferation.

Abnormal blood coagulation.

Patients with blood disease.

Panretinal photocoagulation within the previous three months

Anti VEGF intravitreal injection within the previous three months

Neovascular glaucoma

Rubiosis iridis

Preoperative Evaluation:

History Taking:

Age and sex.

Duration and type of diabetes mellitus (type 1 or 2), drugs used for control of blood glucose level, as well as the current status of glycemic control.

Onset, course and duration of visual complaints (diminution of vision, floaters and/or photopsia).

Past history of ocular diseases, ocular trauma, previous laser therapy or previous ocular surgery.

Past history of systemic diseases especially hypertension, renal or cardiac diseases and abnormal blood coagulation

Extensive Examination of the Eyes:

A visual acuity test using the Landolt C chart

Anterior segment examination with a biomicroscope and a slit lamp. Corneal and IOL optical clarity as well as rubeosis iridis are all factors to consider when diagnosing an eye disease or eye defect.

Measurement of intraocular pressure using Goldmann applanation tonometer.

Fundus examination using indirect ophthalmoscope or slit lamp biomicroscope utilizing A fundus lens that does not touch the eye (+78D, +90D).

B-scan ultrasonography for all patients.

Follow-up:

First postoperative day, first postoperative week, first postoperative month, and then third postoperative month were all scheduled follow-up appointments for all patients.

Postoperative visits included the following procedures for each patient:

Using the Landolt C chart, the best corrected visual acuity can be determined.

Using a slit lamp biomicroscope, the anterior segment is examined. Anterior chamber edema and the increase of lens opacity are indicators of corneal edema and anterior chamber response.

Measurement of Intraocular Pressure using Goldmann applanation tonometer.

Fundus Examination using indirect ophthalmoscope or slit lamp biomicroscope utilizing A fundus lens that does not touch the eye (+78D, +90D).

B-scan ultrasonography for all patients

Prior and postoperative vitreous hemorrhage (VH) severity was defined:

Grade I: (optic disc, retinal vessels and macula are visible).

Grade II: (optic disc and retinal vessels are visible while macula is invisible).

Grade III: (optic disc is visible while retinal vessels and macula are invisible).

Grade IV: (optic disc, retinal vessels and macula are invisible) [(2)].

VH recurrence within the first month following surgery is characterized as early rebleeding.

Late postoperative VH: has been characterized as post-operative VH that occurs between one month and three months after surgery [(3)].

Surgical Technique:

Three-port Pars Plana Vitrectomy:

Maximum pupillary dilation was obtained by topical application of tropicamide 1% (Mydriacyl®) eye drops. All patients were operated upon under local anaesthesia, after proper control of their glycemic status.

Incisions and Creation of Sclerotomies:

The conjunctiva over the intended sclerotomy site was displaced with a cotton-tipped applicator or forceps. A 30-degree scleral tunnel was drilled in the inferotemporal, superonasal, and superotemporal quadrants using a sharp trocar with a mounted cannula. Cannula and trocar were both removed from the patient. There were two sets of cannulas used for microsurgical tools: one for the infusion of fluid and one for the insertion of microsurgical instruments.

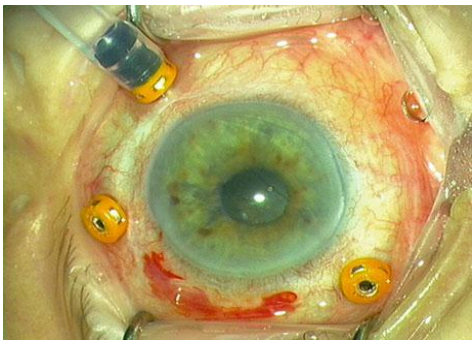

Fig. 1: Sclerotomies in 23-gauge PPV.

Pars Plana Vitrectomy :

All surgeries were performed using DORC vitrectomy machine and Stellaris vitrectomy machine. An operating microscope (Zeiss) equipped with focusing, zoom magnification, as well as an X-Y drive system was the primary method of visualization. Non-contact wide-angle viewing was achieved by attaching a binocular indirect ophthalmic microscopy (BIOM) to the operating microscope oculars. The vitrectomy probe and the fiberoptic endoilluminator were introduced through the superior sclerotomies. After a core vitrectomy, the vitrectomy probe was used to make a hole in the posterior hyaloid that linked the preretinal region with the vitreous cavity. Preretinal blood was aspirated with a soft-tipped flute needle or with active suction of the vitrectomy probe. The posterior hyaloid was then excised for 360 degrees. If required, intravitreal injection of triamcinolone acetonide suspension (Kenacort®) was done to aid visualization of the posterior hyaloid. To alleviate anteroposterior

traction, a peripheral vitrectomy was performed. To remove as much blood as feasible, we used aided scleral depression and shaved the vitreous base. Segmentation and delamination procedures were used to remove epiretinal membranes as well as fibrovascular tissue to alleviate tangential traction. Endodiathermy or intraocular pressure were used to maintain hemostasis. As part of the endolaser photocoagulation, ora serrata was completely eliminated. Exchange of fluids and air occurred.

Closure of Sclerotomies :

In 23-gauge PPV, the two superior cannulas were plugged before removal then they were grasped with forceps and withdrawn along the direction of the scleral tunnel. Gentle pressure was applied for few seconds to the sclerotomy sites using a cotton-tipped applicator, a minor shift in the conjunctiva above the Sclerotomy disrupted the alignment of both entry points. To ensure watertight closure of the sclerotomy wound, a single 7-0 vicryl suture was inserted across both conjunctiva and sclera. Lastly, the inferotemporal cannula, together with the infusion line, was removed in the same way.

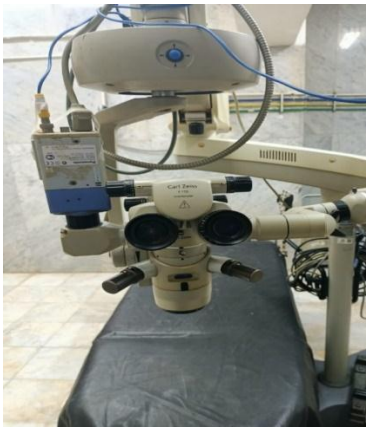

Fig. 2: Zeiss operating microscope.

Fig. 3: BIOM.

Fig. 4: DORC vitrectomy machine.

Fig. 5: Stellaris vitrectomy machine.

Group (b): Injection of ranibizumab before operation

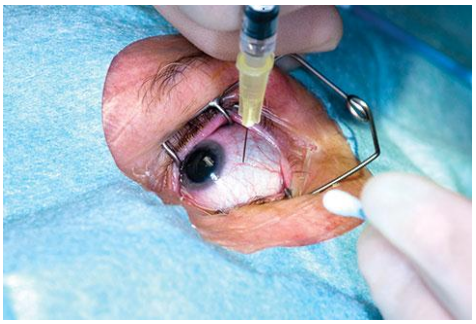

Fig. 6: Intravitreal injection of anti-VEGF group.

Postoperative Management :

Eye drops of 0.5 percent moxifloxacin and 1 percent tropical prednisolone acetate were used for the first two weeks of postoperative treatment, and cycloplegic eye drops were used for one week.

Statistical analysis :

IBM SPSS version 20 was used to collect and analyse the data, which were reviewed, coded and entered into the database. quantitative data were displayed as mean, standard deviations and ranges when their distribution was parametric; qualitative data were given as numbers and percentages.

A chi-square test was used to compare two groups based on qualitative data. Based on quantitative data and parametric distributions, Independent t-tests were used to compare two independent groups.

The significance of the p-value was determined as follows :

Non-significant (NS) results have a p-value of higher than 0.05 .

significant (S) results have a p-value of less than 0.05 .

High-significant (HS) results have a p-value of lower than 0.001.

RESULTS

This research used 40 pairs of eyes in all. PDR-related problems necessitated the use of PPV in all cases (severe non-clearing vitreous hemorrhage).

There were two groups of eyes that were considered eligible: Twenty eyes in Group A had no intravitreal injections, while twenty eyes in Group B received a ranibizumab intraoperative intravitreal injection.

Demographic and clinical data:

Patients were between the ages of 45 and 65. Group A and Group B had the mean averages of age as 55.35±5.40 and 55.8 ±4.97 years, respectively. Both groups were found to be statistically indistinguishable (p-value = 0.0818). As for gender, there was no statistically significant difference between Groups A and B in terms of 50% and 60% male patients (P=0.525).

Regarding the type and duration of diabetes mellitus in each group, the mean of duration of DM in Group A and B was 16.6±6.31and 20.6± 5.67, respectively P-values of (P=0.429) and (P=0. 147) for type and duration of DM were found to be statistically insignificant.

Regarding hypertension, the mean of duration of hypertension in Group A and B was 15.8±5.09 and 12.75±5.49, respectively in each category, A statistically insignificant difference (P=0.204) was found between the two groups.

Regarding lens status,

In Group A, 2 eyes (35%) were pseudophakic, 5 eyes (15%) had clear lens, while 3 eyes (50%) had some degree of cataract.

In Group B, 3 eyes (25%) were pseudophakic, 4 eyes (20%) had clear lens, while 3 eyes (55%) had some degree of cataract, P=0.770 indicates that there is no statistically significant difference between the two groups.

Regarding history of PRP before three months preoperatively, 50 % and 35 % of patients had previous PRP before three months in Group A and B, respectively, The two groups were statistically indistinguishable (P=0.325) (Table 1).

Variables	Studied groups		
	Group A no IVR injection N =20 100%	Group B IVR injection N=20 100%	Test of significance
Sex:			Chi-sq=0.404
Male	10(50%)	12(60%)	P=0.525
Female	10(50%)	8(40%)	
Type of DM:			Chi-sq=0.625
Type I DM	5(25%)	3(15%)	P=0.429
Type II DM	15(75%)	17(85%)	
Duration of DM:			Chi-sq=3.833
≤10 ys	3(15%)	1(5%)	P=0.3372
≥20 ys	9(45%)	15(75%)	
10-20 ys	8(40%)	4(20%)	
Hypertension:			Chi-sq=0.100
Yes	9(45%)	10(50%)	P=0.752
No	11(55%)	10(50%)	
lens status anterior seg examination:			Chi-sq=0.524
Clear lens	3(15%)	4(20%)	P=0.770
Some degree of cataract	10(50%)	11(55%)	
Pseudophakia	7(35%)	5(25%)	
Age			Chi-sq=0.930
45-50yrs	3(15%)	2(10%)	P=0.818
50-55yrs	5(25%)	7(35%)	
55-60yrs	8(40%)	6(30%)	
60-65yrs	4(20%)	5(25%)	
Duration of HTN			Chi-sq=3.182
≥10yrs	5(25%)	7(35%)	P=0.204
10-20yrs	10(50%)	12(60%)	
≤20yrs	5(25%)	1(5%)	
History of PRP:			Chi-sq=0.921
Yes	10(50%)	7(35%)	P=0.337
No	10(50%)	13(65%)	
	Mean± Std. Deviation		
Age	55.40±4.142	54.40±3.169	t=.606 P=0. 552
Duration of DM	17.10±7.852	15.90±5.109	t=.405 P=0. 690
Duration of hypertension	5.00±3.391	4.167±2.563	t=.465 P=0. 653

Table 1: The demographic and clinical data

Preoperative Best Corrected Visual Acuity (BCVA) Among the studied groups:

Variables	Studied groups		
	Group A no IVR injection N=20 100%	Group B IVR injection N=20 100%	Test of significance
Pre-BCVA:			
-<0.5-1	1(5%)	1(5%)	Chi-sq=0.487
1-1.8	5(25%)	7(35%)	P=0.784
->1.8	14(70%)	12(60%)	

Table 2: Comparison between the preoperative BCVA among the studied groups

Table 2 shows the preoperative BCVA is >1.8 in 14 eyes in (70%) of group A and >1-1.8 in 7 eyes (35%) of group B. (P=0.784) This was not statistically significant.

≤0.5 logMAR corresponds to ≥6/18 Snellen equivalent.

>0.5 – 1.0 logMAR corresponds to 6/60 – <6/18 Snellen equivalent.

>1.0 – 1.8 logMAR corresponds to 1/60 – <6/60 Snellen equivalent.

>1.8 logMAR corresponds to <1/60 Snellen equivalent.

Variable	Studied groups	N	Mean	Std. Deviation	T	p-value
Pre-BCVA (Log MAR)	Group A no IVR injection	20	1.98	0.213	4.240	0.000138
	Group B IVR injection	20	1.68	0.234		

Table 3: Mean difference between the studied groups as regard pre-BCVA (Log MAR)

This table illustrate the mean difference between both groups regarding preoperative BCVA (log Mar) in which (t test =4.240) and no significant change (p> 0.05) was seen.

Postoperative Best Corrected Visual Acuity (BCVA) Among two studied groups:

Variables	Studied Groups	N	Mean	Std. Deviation	T	P-value
Post BCVA 1 week	Group A no IVR injection	20	1.099	0.1232	0.2023	0.8407
	Group B IVR injection	20	1.091	0.1269		
Post BCVA *1 month	Group A no IVR injection	20	1.027	0.1012	0.8337	0.4097
	Group B IVR injection	20	1.000	0.1036		
Post BCVA *3 months	Group A no IVR injection	20	0.942	0.1281		
	Group B IVR injection	20	0.810	0.0788	3.9251	0.0004

Table 4: Mean difference between the studied groups as regard post-BCVA (Log MAR)

This table shows the mean postoperative BCVA (log MAR) among the studied groups at 1 week, 1month and 3months where the mean difference between both groups at 3months postoperatively (t =3.925and p=0.0004). This difference is statistically significant. One week and one month after surgery, there is no statistically significant difference between the groups.

In the study, the paired t-test was used to compare mean differences between the pre-BCVA (Log MAR) and post-BCVA (Log MAR) groups:

Variable	N	Mean	Std. Deviation	T	Sig.p (2-tailed)
Pre-BCVA (Log MAR) - post BCVA 1 Week	40	0.734	0.352	18.27	0.000

Table 5: Differences in mean pre-BCVA (Log MAR) vs. following (Log MAR) outcomes among the study groups at one-week post-BCVA

This table shows mean BCVA (log MAR) improved to 0.734±0.352 (p = 0.000) across the tested groups after one week of treatment, with a statistically significant difference between the two groups.

Variable	N	Mean	Std. Deviation	T	Sig. (2-tailed)
Pre-BCVA (Log MAR) - post BCVA 1 month	40	0.816	0.385	21.103	0.000

Table 6: One month after the study, the mean differences between pre-BCVA (Log MAR) and post-BCVA (Log MAR) across the analyzed groups

This table shows pre-and post-BCVA (Log MAR) 1 month mean differences were 0.816±0.385, which is a statistically significant difference between groups (p = 0.000).

Variable	N	Mean	Std. Deviation	T	Sig. (2-tailed)
Pre-BCVA (Log MAR) - post BCV A 3 months	40	0.953	0.451	23.678	0.000

Table 7: Pre-BCVA (Log MAR) to post-BCVA (Log MAR) differences across the study groups at 3 months after treatment

This table shows the Pre-BCVA (Log MAR) differences between the examined groups at 3 months were statistically significant (p = 0.000) and the difference between the two groups was 0.953±0.451.

Post-operative complications:

Variables	Studied groups		
	Group A no IVR injection N=20 100%	Group B IVR injection N=20 100%	Test of significance
Incidence of post V.H 1 week			
Clear	13(65%)	15(75%)	Chi-sq=0.476
V.H	7(35%)	5(25%)	P=0.490
Incidence of post V.H 1 Month			
Clear	14(70%)	16(80%)	Chi-sq=0.533
V.H	6(30%)	4(20%)	P=0.465
Incidence of post V.H 3Months			
Clear	16(80%)	19(95%)	Chi-sq=2.057
V.H	4(20%)	1(5%)	P=0.151
Cataract progress:			
Not progress	14(70%)	12(60%)	Chi-sq=0.440
Progress	6(30%)	8(40%)	P=0.507

Table 8: Post operative complication

This table shows No statistically significant difference between the two groups in the incidence of post-operative vitreous hemorrhage at one week, one month, and three months (P>0.05).
Six eyes (30%) and eight eyes (40%) exhibited cataract progression in group A and group B, with no statistically significant difference (P=0. 507) in the two groups.

DISCUSSION

The rate of postoperative recurrent vitreous hemorrhage following PPV for proliferative diabetic retinopathy (PDR) ranges from 29 percent to 75 percent, according to the American Diabetes Association. [4].

Complications such as these impede visual rehabilitation and may demand additional surgical treatments. There are several possible causes, but the most common is the spread of leftover blood from the peripheral vitreous skirt into the vitreous cavity, remains of fibrovascular tissues, and surgical iatrogenic damage to retinal blood vessels, Sclerotomy sites, anterograde fibrovascular growth, and neovascularization of the angle of the eye all contribute to late postoperative VH development [1].

Among the United States, diabetes is a leading cause of vision loss in working-age persons. This type of diabetic retinopathy is associated with visual loss of less than 5/200 (acuity). There is a well-accepted treatment for proliferative diabetic retinopathy, pan retinal photocoagulation (PRP), which is efficient but has recognized adverse effects such as peripheral vision field limitations. Vascular endothelial growth factor (VEGF) is regarded to be the driving force behind the proliferation of new blood vessels. Diabetic macular edema has been widely examined with anti-VEGF drugs, and the results demonstrate that diabetic retinopathy improves while using these drugs. [5].

Researchers believe that VEGF is an angiogenic mitogen, and investigations have shown that VEGF contents were considerably raised both in the vitreous and aqueous fluids of patients with active PDR compared to samples from patients without diabetes, with NPDR, or with quiescent PDR [6] and PDR patients' fibrovascular tissues were shown to contain VEGF [7].

Preoperative IVR has been shown to cause quick regression of retinal neovascularization, which facilitates fibrovascular membrane dissection, reduces intraoperative hemorrhage and surgical time, and reduces early postoperative VH.

Ranibizumab intravitreal injection could reduce surgery time and intraoperative complications [8].

In our study, we aimed to examine the efficacy of preoperative IVR injection in reducing early postoperative vitreous hemorrhage following pars plana vitrectomy for complications of PDR.

Preoperative administration of IVR did not significantly lower the incidence of postoperative VH in this trial, as demonstrated by a comparison between the two groups. However, lower the intensity and frequency of VH recurrence.

The incidence of post-operative VH was 35 percent in Group A and 25 percent in Group B (p=0.490) at one week following surgery. Group B has a decreased incidence of VH, albeit not statistically significant.

The incidence of postoperative VH was 30 percent in Group A and 20 percent in Group B (p = 0.465) at one month following surgery. Group B has a decreased incidence of VH, albeit not statistically significant.

The incidence of postoperative vitreous haemorrhage was 20% for group A and 5% for group B (P=0.151) at the third month following surgery. A statistically insignificant number of people have experienced this. But statistically is going to be significant but this result (non-significance) was owing to the few numbers of cases. As can be expected, mild VH resulted in mild visual deterioration during its presence and also cleared up much faster, having relatively little impact on the final visual outcome.

In our study, 20% of group A and 5% of group B had postoperative vitreous haemorrhage at the 3rd month (P=0.151). This is not a statistically significant occurrence. Complete elimination of fibrovascular tissue and thorough hemostasis may also have led to a lower incidence of early postoperative VH independent of the use of IVR.

Our study agrees with Chen et al. [9] studyTo reduce intraoperative and early post-vitrectomy hemorrhage, IVR pretreatment should be recommended for young patients with PDR. However, intraoperative and postoperative problems are not reduced by IVR in these patients, IVR, on the other hand, does not minimize the risk of problems during and following surgery in these individuals. In the IVR group, the overall surgical time was less than in the control group.

There was a significant reduction in the incidence of postvitrectomy bleeding (P0.001) in the IVR group as compared to the control group (P=0.03) [9].

Also, our study agrees with Comyn et al. [10] Patients with advanced proliferative diabetic retinopathy who have vitrectomy surgery benefit from pretreatment with ranibizumab, which reduces postoperative vitreous cavity haemorrhage. However, it appears to have a relatively small impact.

Also, our study agrees with Zhao et al. [11] study It is possible that pretreatment with anti-VEGF medicines prior to vitrectomy could make surgery and visual rehabilitation easier and better for patients with difficult PDR, decrease the frequency of early recurrence of VH and speed up absorption.

Also, our study agrees with Pakzad-Vaezi et al. [12] study. Patients with PDR undergoing PPV are treated with intravitreal bevacizumab or ranibizumab as surgical adjuvants, and the results are the same in both cases.

Also, our study agrees with Liang et al. [13] Postoperative diabetic vitreous hemorrhage is prevented by intravitreal ranibizumab injection in eyes having pars plana vitrectomy for the treatment of diabetes.

The intravitreal ranibizumab (IVR) group had a rebleeding rate of 6.1 percent, compared to 24.3 percent in the control group (P.01).

Postoperative diabetic vitreous hemorrhage (PDVH) incidence was considerably lower in the IVR group than in the control group following surgery.

A 0.05-mg intravitreal injection of ranibizumab was given to patients at the end of surgery [13].

In the current study, All study groups' mean BCVA changed significantly from the preoperative BCVA after one week, one month, and three months (p=0.000). the first week and first month after surgery, a comparison of the two groups' BCVAAt 1 week and 1 month postoperatively, there is no statistically significant difference between the two groups, however at 3 months postoperatively, there is a mean difference between the two groups (t =3.925and p=0.0004). That agree with Nowacka et al. [14].

Before and after therapy with ranibizumab, diabetic macular edema patients' vision has improved. Visual acuity and macular thickness improvement lasted for six months after treatment. Ranibizumab injections appear to stabilize bioelectrical macular function in the outer, middle, and inner retinal layers, according to electrophysiological studies. [14]. That agree with Santos et al. [15].

Spectral-domain OCT can identify the best candidates for intravitreal ranibizumab treatment based on the degree of CRT reduction and predict BCVA improvement after treatment.

It was revealed that the degree of CRT drop was linked to the improvement in BCVA [15]. Our study agrees with Guan et al. [16].

Prior to PPV with ILM peeling for severe PDR with ME, ranibizumab may enhance outcomes by reducing ME and intraoperative complications.

In the IVR group, the BCVA at 1, 3, and 6 months was considerably better than the preoperative BCVA (P 0.01). Preoperative BCVA was significantly worse in the control group (P 0.01), however at 3 and 6 months, the BCVA of the control group had dramatically improved, after a month, the situation had not improved appreciably. BCVA was significantly higher in the IVR group than in the control group after surgery at 1 and 3 months, but there was no difference between the two groups at 6 months. Compared to the control group, the IVR group had a thinner CMT at 1 and 3 months, but there was no change at 6 months. There was a significant difference between the two groups in terms of surgical duration, intraoperative bleeding risk, iatrogenic retinal break incidence, endodiathermy frequency, and silicone oil tamponade rate (all P 0.05). In terms of postoperative complications, there was no discernible difference between the two groups [16].

Proliferative diabetic retinopathy patients with mild and moderate VH may benefit from intravitreal ranibizumab injections.

The ranibizumab group had significantly better visual acuity assessments throughout all follow-up visits ($P \leq 0.04$). [17].

Our study agrees with Chen et al. [9] studyTo reduce intraoperative and early post-vitrectomy hemorrhage, IVR pretreatment should be recommended for young patients with PDR. The degree of intraoperative bleeding in the IVR group was considerably lower than in the control group (P=0.04), however IVR does not diminish the occurrence of intraoperative and postoperative problems in these patients. Compared to the control group, the IVR group had a shorter overall surgical time.

Hemorrhage in the early post-vitrectomy period was less common in the IVR group than in the control group, Compared to the control group, early visual recovery in the IVR group was found to be significantly better (P=0.03) [9].

A pre-vitrectomy anti-VEGF medication for difficult PDR patients may lead to more efficient surgery and improved vision recovery, speed up the absorption of early recurrences of VH As a result of pretreatment with anti-VEGF, postoperative best corrected visual acuity was shown to be improved (P<0.05), Less frequent (P<0.05) recurrent vitreous haemorrhage (VH) and faster absorption of subsequent VH [11].

One of the most common post-vitreoretinal surgical problems is the development or growth of a cataract, and if this occurs, a second procedure to remove the cataract is required.

The reported incidence of cataract following vitrectomy ranges from 17% to 80%, depending on the study [18]. A number of factors, including age of the patient, the indication for vitrectomy, the use of intraocular gas or silicone oil tamponade, and the length of follow-up, can influence the rate of cataract formation following vitrectomy. According to another study that looked at the eyeballs of 301 people, those over the age of 50 showed a 6-fold increase in cataract development, while intraocular gas use increased nuclear sclerosis advancement by 60%. [19]. It is possible to completely prevent the formation of cataracts by using silicone oil tamponade [20]. Cheng et al. [21] reported that At 2 years after vitrectomy for a macular hole, the incidence of nuclear sclerosis progression was 100%, and the duration of surgery had no effect on the risk of cataract advancement.

There were six eyes (30 percent) and eight eyes (40 percent) with cataract advancement in group A and group B, with no statistically significant difference between the two groups (P=0. 507).

All eyes which were studied, were left on air tamponade to exclude the bias of tamponading effect of gases or silicon oil.

CONCLUSION

Prior intravitreal ranibizumab injection has lowered postoperative vitreous bleeding following pars plana vitrectomy for complications of PDR**. .**

Mild vitreous hemorrhage is the major component of early postoperative vitreous hemorrhage after surgery, irrespective of preoperative intravitreal ranibizumab injection**.**

The incidence of postoperative vitreous hemorrhage is lower in patients who received preoperative intravitreal ranibizumab injection than in patient that did not receive IVR injection. In spite of this relation between the two groups was not statistically

significant, but this owing to the few numbers of cases in current study

It is safe and well-tolerated to utilize preoperative intravitreal ranibizumab injection for complications of PDR as an adjunct to pars plana vitrectomy.

Despite intravitreal ranibizumab injection, cataract development or advancement is prevalent following pars plana vitrectomy for complications of PDR.

REFERENCES

1. Hershberger VS, Augsburger JJ, Hutchins RK, et al. Fibrovascular ingrowth at sclerotomy sites in vitrectomized diabetic eyes with recurrent vitreous hemorrhage: ultrasound biomicroscopy findings. *Ophthalmology*, 2004; 111(6): 1215-21. doi.org/10.1016/j.ophtha.2003.08.043.
2. Nussenblatt RB, Palestine AG, Chan CC, et al. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. *Ophthalmolgy*. 1985; 92: 467. doi.org/10.1016/S0161-6420(85)34001-0.
3. Smith JM, Steel DH. Anti-vascular endothelial growth factor for prevention of postoperative vitreous cavity haemorrhage after vitrectomy for proliferative diabetic retinopathy. *Cochrane Database Syst Rev*. 2015; CD008214. DOI: 10.1002/14651858.
4. Tolentino FI, Cajita VN, Gancayco T, et al. Vitreous hemorrhage after closed vitrectomy for proliferative diabetic retinopathy. *Ophthalmology*, 1989; 96(10): 1495-500. doi.org/10.1016/S0161-6420(89)32700-X
5. Zhao Y, Singh RP. The role of anti-vascular endothelial growth factor (anti-VEGF) in the management of proliferative diabetic retinopathy. *Drugs in Context*. 2018; 7: 212532. DOI: 10.7573/dic.212532.
6. Selim KM, Sahan D, Muhittin T, Osman C, et al. Increased levels of vascular endothelial growth factor in the aqueous humor of patients with diabetic retinopathy. *Indian J Ophthalmol*., 2010; 58(5): 375-9. DOI: 10.4103/0301-4738.67042.
7. Matsuoka M, Ogata N, Minamino K, et al. Expression of pigment epithelium-derived factor and vascular endothelial growth factor in fibrovascular membranes from patients with proliferative diabetic retinopathy. *Jpn J Ophthalmol*., 2006; 50(2): 116-20. DOI: 10.1007/s10384-005-0294-9.
8. Dong F, Yu C, Ding H, Shen L, et al. Evaluation of intravitreal ranibizumab on the surgical outcome for diabetic retinopathy with tractional retinal detachment. *Medicine*. 2016; 95(8): 2731-35. DOI: 10.1097/MD.0000000000002731.
9. Chen HJ, Wang CG, Dou HL, et al. Effect of intravitreal ranibizumab pretreatment on vitrectomy in young patients with proliferative diabetic retinopathy. *Annals of Palliative Medicine*. 2020; 9(1): 82-9. DOI: 10.21037/apm.2020.01.10.
10. Comyn O, Wickham L, Charteris DG, et al. Ranibizumab pretreatment in diabetic vitrectomy: a pilot randomised controlled trial (the RaDiVit study). *Eye.* 2017; 31(9): 1253-8. DOI: 10.1038/eye.2017.75.
11. Zhao XY, Xia S, Chen YX. Antivascular endothelial growth factor agents pretreatment before vitrectomy for complicated proliferative diabetic retinopathy: a meta-analysis of randomised controlled trials. *British Journal of Ophthalmology*. 2018; 102(8): 1077-85. DOI: 10.1136/bjophthalmol-2017-311344.
12. Pakzad-Vaezi K, Albiani DA, Kirker AW, et al. A randomized study comparing the efficacy of bevacizumab and ranibizumab as pre-treatment for pars plana vitrectomy in proliferative diabetic retinopathy. Ophthalmic Surgery, *Lasers and Imaging Retina*. 2014; 45(6): 521-4. DOI: 10.3928/23258160-20141118-06.
13. Liang X, Zhang Y, Wang JX, et al. Intravitreal ranibizumab injection at the end of vitrectomy for diabetic vitreous hemorrhage (Observational Study). *Medicine*. 2019; 98(20): 517-523. DOI: 10.1097/MD.0000000000015735.
14. Nowacka B, Kirkiewicz M, Mozolewska-Piotrowska K, et al. The macular function and structure in patients with diabetic macular edema before and after ranibizumab treatment. *Documenta Ophthalmologica*. 2016; 132(2): 111-22. DOI: 10.1007/s10633-016-9531-4.
15. Santos AR, Gomes SC, Figueira J, et al. Degree of decrease in central retinal thickness predicts visual acuity response to intravitreal ranibizumab in diabetic macular edema. *Ophthalmologica*. 2014; 231(1): 16-22. DOI: 10.1159/000355487.
16. Guan J, Cai N, Liu LM, et al. Ranibizumab pretreatment in vitrectomy with internal limiting membrane peeling on diabetic macular edema in severe proliferative diabetic retinopathy. *Diabetes Therapy*. 2020; 11(6): 1397-406. DOI: 10.1007/s13300-020-00822-0.
17. Chelala E, Nehme J, El Rami H, et al. Efficacy of intravitreal ranibizumab injections in the treatment of vitreous hemorrhage related to proliferative diabetic retinopathy. *Retina*. 2018; 38(6): 1127-33. DOI: 10.1097/IAE.0000000000-001673
18. Cherfan GM, Michels RG, de Bustros S, et al. Nuclear sclerotic cataract after vitrectomy for idiopathic epiretinal membranes causing macular pucker. *Am J Ophthalmol*. 1991; 111(4): 434-8. doi.org/10.1016/S0002-9394(14)72377-3.
19. Thompson JT. The role of patient age and intraocular gas use in cataract progression after vitrectomy for macular holes and epiretinal membranes. *Am J Ophthalmol*. 2004; 137(2): 250-7. DOI: 10.1016/j.ajo. 2003.09.020.
20. Federman JL, Schubert HD. Complications associated with the use of silicone oil in 150 eyes after retina-vitreous surgery. *Ophthalmology*. 1988; 95(7): 870-6. DOI: 10.1016/s0161-6420(88)33080-0.
21. Cheng L, Azen SP, El-Bradey MH, et al. Duration of vitrectomy and postoperative cataract in the vitrectomy for macular hole study. *Am J Ophthalmol*. 2001; 132(6): 881-7. DOI: 10.1016/s0002-9394(01)01263-6.