Original article

Outcome of pars plana vitrectomy with pre-operative intra vitreal bevacizumab in diabetic patients with vitreous haemorrhage

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ABSTRACT

Background: Intravitreal bevacizumab causes regression of retinal neo vessels in proliferative diabetic retinopathy as it is anti-vascular endothelial growth factor (anti VEGF). So this study was done to observe the effect of pre-operative intravitreal bevacizumab on intra operative outcome when administered in patients with vitreous hemorrhage undergoing pars-plana vitrectomy (PPV).

Patients and methods: This quasi-experimental trial was carried out in the Department of Ophthalmology Services Hospital Lahore from June 2020 to December 2020. Fifty seven diabetic patients with vitreous hemorrhage were selected who were eligible for PPV. Patients with recurrent hemorrhage were not included. Demographics were recorded and all patients were given intravitreal bevacizumab (1.25 mg/0.05 ml) one week prior to vitrectomy and intra-operative bleeding was noted. Intra-operative bleeding was graded as No, Mild and Severe bleeding.

Results: The mean age of patients undergoing PPV was 55.36 ± 4.62 years. There were 35 (61%) males and 22 (39%) females. The mean duration of diabetes was 10.35±1.92 years. Out of 57 eyes, 36 (63.15%) had no bleeding, 11 (19.29%) had mild and 10 (17.54%) had severe intra-operative bleeding.

Conclusion: Intravitreal bevacizumab prior to PPV is quite effective in reducing the risk of intra-operative bleeding in patients with vitreous hemorrhage.

Keywords

Intravitreal bevacizumab, Vitreous hemorrhage, Vitrectomy, Advanced diabetic eye disease

INTRODUCTION

Diabetic retinopathy is an important and common cause of visual impairment among age group of 20 to 64 years.[1] Studies have shown that diabetic retinopathy is present in 15.3-28.9% of patients having diabetes mellitus.[2, 3] According to a study conducted in Gaddap, advanced diabetic eye disease has prevalence of 1.74% among the patients of diabetic retinopathy.[4] Advanced diabetic eye disease is defined by a dense and non-resolving vitreous haemorrhage or tractional retinal detachment or both.[5]

Advanced diabetic eye disease is caused by retinal ischemia that leads to retinal neo-vascularization. Vitrectomy was done for vitreous hemorrhage secondary to diabetes for the first time in 1970.[6] Intra-vitreal Bevacizumab given preoperatively reduces the chances of bleeding during vitrectomy.[7, 8] Bevacizumab is known to be an effective anti-VEGF agent. In the management of neo-vascular age related macular degeneration, it is effectively being used.[9, 10]

A study conducted by Faisal et al., showed that patients who received intravitreal injection Bevacizumab 1.25mg/0.05ml, seven days before undergoing three ports pars-plana vitrectomy had no bleeding in 60.7% of patients whereas 21.4% had mild and 17.9% had severe bleeding which required diathermy. While in routine, when patients underwent surgery without Bevacizumab no bleeding was observed in only 2 cases (7.1%), mild in 6 cases (21.4%) and severe in 20 cases (71.4%).[11]

The rationale of this study was to demonstrate effectiveness of intravitreal injection of Bevacizumab prior to vitrectomy so that the potential intraoperative bleeding can be reduced during vitrectomy of diabetic patients. By reducing intra-operative bleeding, duration of surgery will be reduced and visibility during surgery will be significantly improved. This clarity will minimize chances for un-prompted retinal tear and multiple other complications.

SUBJECTS AND METHODS

This quasi-experimental trial was approved by local Institutional Review Board. This study was carried out in the department of Ophthalmology Services hospital

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Lahore from June 2020 to December 2020 in which fifty seven patients were selected by keeping 95% confidence level, 101% margin of error and percentage of severe intraoperative bleeding i.e. 17.9%,[11] who were candidates for vitrectomy. Both genders between 40-70 years of age were included with vitreous hemorrhage. All the patients who fulfilled the above-mentioned inclusion criteria were informed verbally and those who were willing to participate were included in study after a written informed consent was signed. However, those with uncontrolled hypertension, previous vitrectomy or vitreous hemorrhage secondary to causes other than diabetes like vasculitis, trauma, coagulation abnormalities were excluded. Patients scheduled for surgery were administered intravitreal injection of Bevacizumab in dose of 1.25 mg/0.05 ml, one week before operation.[11] Injection Bevacizumab was given using 29-gauge needle, 3.5mm from limbus (pseudophakia) or 4.0mm from limbus (phakic) after topical anesthesia under sterile conditions in operation theatre. One experienced surgeon administered all the intravitreal injections of Bevacizumab. After a week of injection Bevacizumab, patients underwent PPV. All PPV were performed by a single trained surgeon using the Constellation Vitrectomy Machine (NGENUITY ® 3D Visualization System). PPV consisted of 1) placement of 23 gauge trocar with valve infero-temporally and infusion line for balanced salt solution, 2) 23-gauge valved trocar insertion in superonasal and superotemporal position, 3) Pars plana Vitrectomy using the vitrectomy probe, 4) intraocular endo-cautery and elevation of balanced salt solution as required, 5) aspiration of residual hemorrhage actively from posterior pole of retina, 6) endo-laser photocoagulation of untreated mid peripheral and peripheral retina as needed, 7) Fluid-gas exchange and vitreous substitute as per requirement, and 8) removal of trocars, wound secured along with subconjunctival injection of 1mg gentamicin and 4mg dexamethasone at the completion of surgery. During the above-mentioned procedure, researcher observed the amount of intra-operative bleeding on vitrectomy machine and it was categorized as nil, mild and severe. “No”, if there was no bleeding during vitrectomy, “mild” bleeding if bleeding occurred but stopped by raising the infusion pressure and categorized as “severe” if intraocular diathermy used to halt bleeding.[11] Nil or mild amount of bleeding was considered as positive outcome.

Statistical analysis was done by using computer software SPSS version 21.0. Percentage and frequency were calculated for qualitative variables like gender, and intra-operative bleeding whereas for quantitative variables like age and duration of diabetes, mean and standard deviation were calculated.

RESULTS

Fifty seven patients were enrolled in this study and all of them were given intravitreal injection Bevacizumab, dose of 1.25 mg/0.05ml, one week before vitrectomy surgery. Mean age of patients was 55.36±4.62 years (range 48-65 years). Out of 57 patients, 35 (61%) are male while 22 (39%) are female. Mean for duration of diabetes in patients was 10.35±1.92 years (range 7-15 years). The mean intraocular pressure was 19.33 ± 7.32 mmHg. BCVA was 6/6 in 7 (12.3%) patients, 6/9 in 17 (29.8%) patients, 6/36 in 12 (21.1%) patients, hand perception in 21 (36.8%) patients. Table 1 summarizes the characteristics of patients.

During procedure, in 63.15% of patients there was no bleeding, in 19.29% there was mild and in 17.54% of patients, severe bleeding was observed.

DISCUSSION

Pre-operative use of intravitreal bevacizumab before pars plana vitrectomy for patients with vitreous hemorrhage has been suggested in the recent years.[12] In a study by Zhao et al, intravitreal anti VEGF regresses diabetic

Table 1. Characteristics of the patients.

Characteristics	Frequency n (%)
Age (years ± SD)	55.36 ± 4.62
Gender	
Male	35 (61%)
Female	22 (39%)
Lateral side	
Left	27
Right	30
Duration of diabetes (years ± SD)	10.35±1.92
Intraocular pressure (mmHg)	19.33 ± 7.32
BCVA	
20/20	7 (12.3%)
20/200	17 (29.8%)
Counting finger	12 (21.1%)
Hand motion	21 (36.8%)

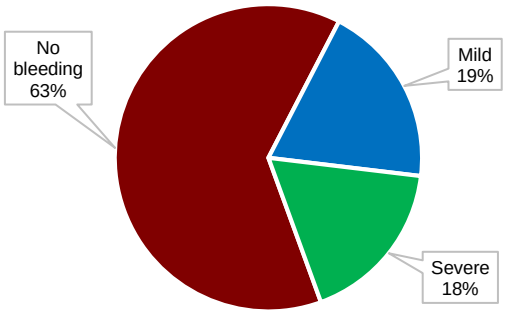

Figure 1. Frequency of Intra operative hemorrhage.

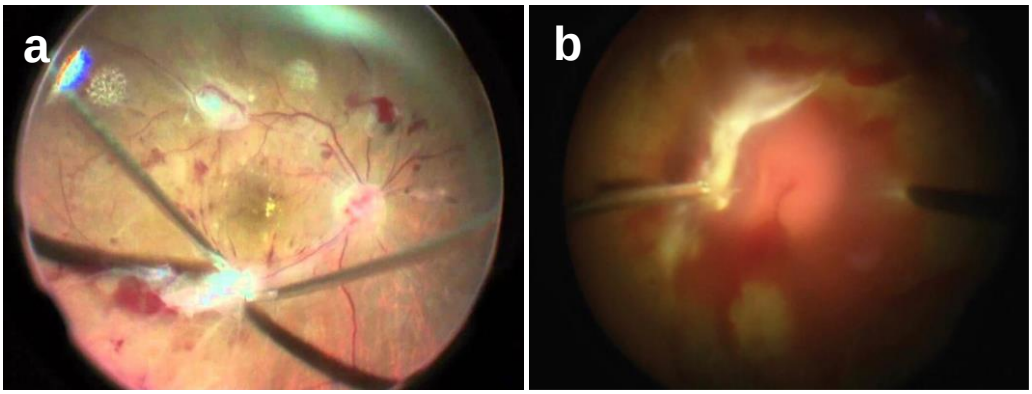

Figure 2. a) Mild intraoperative bleeding, b) severe intraoperative bleeding.

retinopathy especially in patients with vitreous hemorrhage where argon laser is not possible due to compromised view.[13]

Chen and park reported a case of diabetic patient with tractional retinal detachment who was administered intravitreal bevacizumab prior to PPV which regressed the new vessels and hence reduced intra operative bleeding which was directly observed.[9] Feng et al advocated PPV in PDR should be done within a week of administration of intravitreal bevacizumab in order to get its maximum effect on vascular neovascularization.[14]

In this study, 55.36 year was mean age (48-65 years). Mostly patients were in their sixth decade of life when they developed advanced diabetic eye disease for which they underwent vitrectomy. According to Rizzo et al, in their study the range for patient's age was from 24 to 63 years with mean age of 52 years.[7] In another study carried out by Zhao et al, mean age of patients was 46 years with range of 28-61 years.[13]

In our study mean duration for diabetes was 10.35 years (with a range of 7-15 years). Mean duration for diabetes was 15 years according to study by Avery et al.,[12] diabetes present for longer duration has direct relation with the prevalence of diabetic retinopathy. In a developing country such as Pakistan, most of our patients belong to the poor socioeconomic status especially those presenting in a public hospital like ours. These patients have poor compliance to medication, poor dietary habits and poor control of diabetes which ultimately leads towards rapid progression and worsening of diabetic retinopathy.

In patients with advanced diabetic eye disease, recurrent bleeding from different proliferative sites can make the surgery lengthy and troublesome which necessitates the use of extensive cautery that may incite post-operative inflammation. Other attempt to stop bleeding by increasing the intraocular pressure may lead to corneal edema eventually hampering surgical visualization. Hence, intravitreal anti VEGF a week prior to surgery that regresses the neovascularization, will decrease intraoperative bleeding, facilitate surgery and decrease the complications of surgery. A few studies showed that it can reduce the incidence of post vitrectomy cavity hemorrhage as well.[15-20]

In our study all patients were given intravitreal bevacizumab one week prior to vitrectomy and then observed for intra operative bleeding. Total 63.15% of patients had no bleeding, 19.29% had mild while 17.54% had severe bleeding in which endo diathermy was being used to stop the bleeding. In study by Rizzo et al, among a group that had received Bevacizumab, no bleeding was noted in 54% of patients, mild bleeding in 27% and severe bleeding was noticed in 18% of patients.[7]

In a similar study conducted by Faisal et al, there was no bleeding in 60.7%,mild in 21.4% and severe in only 17.9% in patients who administered intravitreal Bevacizumab pre-operatively.[11] Another study by Nagpal et al., also observed 56.6% patients with no bleeding, 21.8 % with mild and 21.8% with severe bleeding in patients who received pre-operative Bevacizumab.[21] In a study by Demir et al and Mota et al, the group which received intravitreal bevacizumab, significant reduction in intraoperative bleeding was observed.[19, 22] Reducing the intra-operative bleeding during vitrectomy significantly reduces the risk of iatrogenic tears and further complications.[15] It is very important to decrease the above-mentioned risks by every possible means.

CONCLUSION

Intravitreal bevacizumab prior to PPV is efficient in reducing active retinal neovascularization, thus reducing the intra operative risk of bleeding. This provides better

outcome of surgery than without Bevacizumab. Thus in future, we can implement the use of Intravitreal bevacizumab prior to PPV to reduce the chances of intraoperative bleeding in >50% cases.

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