

ORIGINAL ARTICLE

Postoperative Bleed after PARS Plana Vitrectomy with Pre-Operative Intra Vitreal Bevacizumab in Diabetic Patients with Advance Diabetic Eye Disease

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ABSTRACT

Objectives: The aim of this study is to investigate the effect of preoperative intravitreal Bevacizumab on postoperative incidence of vitreous cavity hemorrhage in patients with advance diabetic eye disease undergoing 23 gauge pars plana vitrectomy.

Study Duration: This study was conducted in the department of Ophthalmology Services Hospital Lahore from April 2021 to September 2021.

Study Design: Randomized Controlled Trail

Patients & Methods: Forty eyes of forty diabetic patients with advance diabetic eye disease were selected for three port 23 gauge pars plana vitrectomy (PPV) and were split into two groups of twenty patients each. One week before the pars plana vitrectomy, Group A received preoperative intravitreal bevacizumab (1.25 mg/0.05 ml) and sham injection were given to Group B patients and postoperative vitreous cavity bleeding was noted on day one , day three , day seven and bleeding was graded from no bleeding to mild and severe based on clinical examination.

Practical implication: To assess the decrease in potential risk of postoperative vitreous cavity bleeding following 23 gauge three port pars plana vitrectomy

Results: The patients in this study had an average age of 58.46 ±3.62 yrs and mean duration of diabetes among these patients selected for this trial was 11.25±1.52 years (range 8-22 years). Out of 20 eyes in Group A , 15 (75.0%) had no bleeding, 4 (20.0%) had mild and 1(5.0%) had severe postoperative vitreous cavity bleed. In group B , out of 20 eyes 11(55.0%) had no bleeding , 7(35%) had mild to moderate bleeding and 2(10.0%) had severe vitreous cavity hemorrhage.

Conclusion: Preoperative Intravitreal bevacizumab prior to pars plana vitrectomy was found effective in reducing the risk of postoperative vitreous cavity bleeding in patients with advance diabetic eye disease.

Keywords: Intravitreal Bevacizumab, advanced diabetic eye disease, vitreous hemorrhage, Postoperative bleed, Vitrectomy

INTRODUCTION

In the working-age population (defined as those between the ages of 20 and 64), diabetic retinopathy is the leading cause of blindness.¹ Studies have shown that some grade of diabetic retinopathy ranging from background or pre proliferative to proliferative and advance diabetic eye disease is present among 15.3-28.9% of patients depending upon demographics and duration of diabetes mellitus that includes various factors like age at the onset of diabetes mellitus and duration of disease but the most important factor being severity of poor glycemic control.^{2,3} Advanced diabetic eye disease according to ETDRS Classification (Early treatment of diabetic retinopathy trial) is defined by non-resolving vitreous hemorrhage and/or tractional retinal detachment in patients with early age of onset , long duration and poor control of diabetes mellitus.^{4,5}

Advanced diabetic eye disease is caused by retinal ischemia which develops due to capillary drop out along with microangiopathic phenomenon which is mediated by abnormalities in Virchow's triad and development of advance glycation end products causing vascular endothelial damage that leads to the development of retinal neo-vascularization under the influence of VEGF (Vascular endothelial growth factor) produced in response to ischemia under control of HIF (Hypoxia inducible factor). These neo vessels are friable , easy to bleed and are leaky blood vessels due to abnormal basement membrane development in these patients in response to metabolic derangements caused by persistent long term hyperglycemia.^{7,8}

Patients with advanced diabetic eye disease who underwent 23 gauge three ports pars plana vitrectomy for tractional retinal detachment and received a preoperative intravitreal inj. of Bevacizumab seven days before surgery had no bleeding in 60.7%, mild bleeding in 21.2%, and excessive bleeding requiring diathermy per operatively in only 17.9% but this study had limited generalization as its sample size was low and there is also due to variation among surgical techniques between different surgeons and case to case variation .¹¹

The rationale of this study is to come up with evidence based data that could guide us in future management of advance diabetic eye disease or.

SUBJECTS AND METHODS

After receiving approval from our local Institutional ethical Review Board, the study term of six months commenced. This research was conducted between April 2021 and September 2021 in Services hospital Lahore's Eye Unit 1. Forty eyes from 40 patients with advanced diabetic eye disease were chosen for 23 gauge three port pars plana vitrectomy, and the patients were split into two groups of 20. Group A received intravitreal bevacizumab (1.25 mg/0.05 ml) one week before pars plana vitrectomy and sham injection were given to Group B patients, our study was a comparative study between group A patients receiving preoperative intravitreal Bevacizumab and group B patients who had sham injection intravitreally before surgery and the results in terms of post operative incidence of vitreous hemorrhage were compared between the two groups.

Patients having tractional retinal detachments or persistent vitreous bleeding for more than three months, despite three intravitreal injections of Bevacizumab or two first-line anti-VEGF administered at monthly intervals for three months, were included. All patients meeting the aforementioned criteria were given a thorough verbal explanation of the study's aims, methods, and selection procedures in the patients' native language.

After seven days of intravitreal injection Avastin (Bevacizumab)/sham injections , patients were operated for three ports pars plana vitrectomy using 23 gauge system. All pars plana vitrectomies in this study were performed by an experienced retinal surgeon and single assistant surgeon on Millennium Vitrectomy Machine with 23 gauge vitrectomy sets. This surgical procedure starts with placement of three valved cannulas with trocars for primary scleral entry points. The inferotemporal cannula is attached with an infusion line to irrigate the vitreous cavity and maintain intraocular pressure during the procedure and maintains

tone of eye ball throughout the procedure and the remaining two ports one superonasal and the other superotemporal are used for endo light source and vitrectomy cutter .A biome viewing system is used that is attached with the operating microscope for this surgery. Initially core vitrectomy is done to clear up the vitreous hemorrhage and obtain a reasonable view of the retina , then with the help of triamcinolone, vitreous or posterior hyaloids face is stained and cleared followed by segmentation and delamination depending upon the type and extend of tractional retinal detachment .Depending upon the status of posterior hyaloid face, an en block dissection of the trational membranes can also be done .After removal of tractional membranes peripheral vitreous shave is carried out and an air fluid exchange is performed followed by injection of silicone oil as a temponading agent and three canullas are removed and ports closed.

During this study we collected data from both groups, group A having the preoperative intravitreal Bevacizumab and Group B having preoperative sham intravitreal injection one week before surgery. Data collection was done by post operative clinical examination of these patients following 23 gauge pars palna vitrectomy on day one , day three and day seven via slit lamp bio microscopy with the help of a 78 D lens. Grading of the vitreous cavity bleeding was performed as no bleed if no clinical evidence of blood both pre retinal and sub retinal ,mild if bleeding was localized at a single point less than one disc diameter and severe if bleeding was found at more than one location with extend of more than one disc diameter . No or mild bleeding was considered as evidence of effectiveness of Bevacizumab injected pre operatively.

RESULTS

In this study, 40 patients were involved. In group A, 20 patients received a preoperative intravitreal injection of Avastin (Bevacizumab) at a dose of 1.25 mg/0.05 ml, while 20 patients in group B received a preoperative intravitreal injection of saline one week prior to undergoing a 23 gauge, three port pars plana vitrectomy surgery. The patients in this study had an average age of 58.46 \pm 3.62 yrs and mean duration of diabetes among these patients selected for this trial was 11.25 \pm 1.52 years (range 8-22 years). Out of 40 patients, 28 (70%) of the 40 patients were men, and 12 (30%), were women. A 18.15 \pm 6.21 mmHg mean intraocular pressure (IOP) was measured. When comparing demographic data (age, gender and duration of diabetes), there was no statistically significant difference between the two groups (P value > 0.05).

Out of 20 eyes in Group A, 15 (75.0%) had no bleeding, 4 (20.0%) had mild to moderate and 1(5.0%) had severe postoperative vitreous cavity bleed. In group B, out of 20 eyes 11(55.0%) had no bleeding, 7(35%) had mild to moderate bleeding and 2(10.0%) had severe vitreous cavity hemorrhage. Group-A had much lower postoperative bleeding than Group-B. (p value 0.001). Table 2 displays a comparison of the bleeding rates of the two groups.

Table 1: Characteristics of the enrolled patients in current research

Characteristics	Variables	Frequency
Age	Mean \pm SD	58.46 \pm 3.62 Years
Gender	Male	28 (70.0%)
	Female	12 (30.0%)
Lateral side	Left	17 (42.53%)
	Right	23 (57.51%)
Diabetes duration	Mean \pm SD	11.25 \pm 1.52 years
	Range	8-22 years
Intraocular pressure	IOP (mmHg)	18.15 \pm 6.21

Table 2: Postoperative bleeding during surgery in Avastin Group A and Control (sham injection) Group B

Characteristics	Variables	Group-A	Group-B
Postoperative Bleeding	No	15 (75.0%)	11(55.0%)
	Mild to Moderate	4 (20.0%)	7(35%)
	Severe	1(5.0%)	2(10.0%)

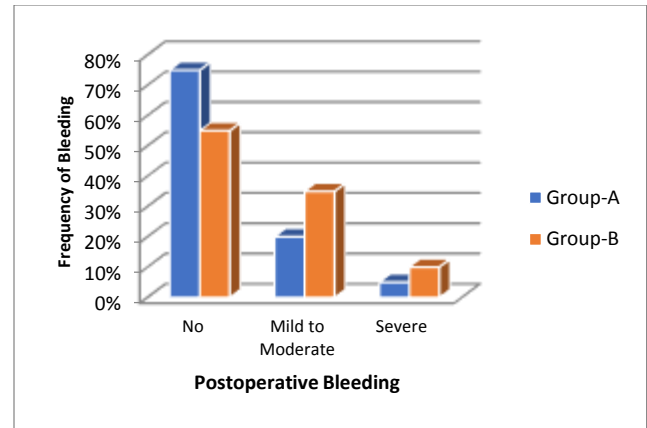


Figure 1: Postoperative bleeding during surgery in Avastin Group A and Control (sham injection) Group B

DISCUSSION

yue et al. have shown in a study that preoperative injection of intravitreal bevacizumab clears the view and cause regression of retinal neo vascularization that would have not been possible by pan retinal photo coagulation using argon laser due to the compromised view caused by dense vitreous haemorrhage.²¹ Case reports by Chen and park have shown effectiveness of preoperative bevacizumab when used intravitreally up to ten days before pars pala vitrectomy showed regression of new vessels and reduced the intra operative bleeding significantly .⁹ Recent studies have shown that the best time to inject preoperative intravitreal bevacizumab to reduce post operative and per operative bleeding in patients undergoing pars plana vitrectomy is seven days , as in these seven days the vascular component of the membranes is regressed and later the fibrous component starts to shrink .¹²

In this study preoperative intravitreal Bevacizumab was injected one week prior to surgery for the reason that Bevacizumab acts on both the vascular and the fibrous component of tractional mambranes in diabetic eye disease but in the first week it acts to reduce the proliferation of new vessels and then regression of these new vessels starts, after one week the fibrous component starts to contract which in certain cases can lead to worsening of tractional retinal detachmemnt and is the reason that par plana vitrectomy should be performed within one weeks of intravitreal Bevacizumab if given preoperatively to reduce per operative and post operative vitreous cavity bleeding.

Duration of uncontrolled diabetes mellitus causes the microangiopathic sates to develop in retinal vasculature which leads to development of compromised retinal hemodynamics that in turn cause capillary drop out and retinal ischemia to develop where there is an imbalance between demand of oxygen and supply by the retinal vasculature , at least one quarter of the retina must be ischemic for the retinal neo vascularization to develop.

Duration of diabetes mellitus is directly correlated with the development of diabetic eye disease as well as its progression from non proliferative to proliferative diabetic retinopathy. Diabetic retinopathy effects vision and is the main cause of significant visual loss or legal blindness among the working age group in developing countries like our own. The main reasons for this are poor compliance to medication either due to lack of awareness or non affordability, poor dietary habits and un balanced nutritional intake and poor control of diabetes that leads to the development of diabetic retinopathy and later on rapid progression of diabetic retinopathy from non proliferative to proliferative and ultimately to advance diabetic eye disease.

In patients with advance diabetic eye disease that undergo 23 guage pars plana vitrectomy , there is a high risk of intra operative and post operative cavity hemorrhage as the sites with neo vascular proliferations are leaky and are easy to bleed with

manipulation during or after surgery thus leading to high incidence of post operative inflammation and bleeding . Therefore the use of pre operative intravitreal anti VEGF like Bevacizumab can reduce not only post operative vitreous cavity bleeding but if given a week can reduce the incidence of intra operative bleeding which can in turn reduce the need of endo cauterization and can provide a better view during surgery leading to reduction in operating time and less post operative inflammation in these cases .¹⁴⁻¹⁹

In a related study, Rizzo et al. found that among patients with advanced diabetic retinopathy who received intravitreal Bevacizumab (Avastin) injections, there was no or minimal bleeding in 54% of cases, mild to moderate bleeding in 27%, and severe bleeding in 18% of patients undergoing pars plana vitrectomy.⁷ Nagpal M et al also reported 56.6% patients with no or minimal post operative bleeding, 22 % of the patients with mild to moderate vitreous cavity hemorrhage and 22 % with severe vitreous cavity hemorrhage in patients with advance diabetic eye disease who received pre-operative intravitrealBevacizumab (Avastin).^{22,13,18} Studies have shown that with the use of bevacizumab intravitreally in patients with advance diabetic eye disease pre operatively, we can reduce the risk of iatrogenic retinal breaks during surgery and can reduce complications from this procedure.^{14,7}

CONCLUSION

In conclusion of our discussion, patients with advance diabetic eye disease undergoing 23 gauge pars plana vitrectomy either for vitreous hemorrhage or tractional retinal detachment , can benefit from the preoperative intravitreal use of Bevacizumab as it reduces the incidence of post operative vitreous cavity bleeding and can reduce the rate of complications from this procedure.

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