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RESEARCH ARTICLE
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POST OPERATIVE BLEED AFTER PARS PLANA VITRECTOMY WITH PRE-OPERATIVE INTRA VITREAL BEVACIZUMAB VS INTRAVITREAL RANIBIZUMAB IN DIABETIC PATIENTS WITH ADVANCE DIABETIC EYE DISEASE

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There is no conflict of interest in this study to declare.

ABSTRACT

Background

Intravitreal Bevacizumab (Avastin) and Ranibizumab (Patizra) both are vascular endothelial growth factor(VEGF) inhibitors that are developed against vascular endothelial growth factor isoforms which is the driving force behind ischemic neo vascularization in diabetic eye disease. The objective of our study is to evaluate the efficacy of pre-operative intravitreal Bevacizumab Vs Intravitreal Ranibizumab on post operative vitreous cavity bleed after three port 23 gauge pars-plana vitrectomy (PPV).

Patients & Methods

This study was conducted in the department of Ophthalmology Services Hospital Lahore from January 2024 to June 2024.Fourty (40) patients with advance diabetic eye disease were included in this study for three port 23 gauge pars plana vitrectomy (PPV) with pre operative intravitreal Bevacizumab or Avastin(1.25 mg/0.05 ml) and Intravitreal Ranibizumab one week prior to PPV and incidence as well as severity of post operative vitreous cavity bleeding was recorded on day

one, day three and day seven along with severity grading from no visible bleed to mild and severe based on fundus examination .

Results

Mean patient age in our study was 57.36±3.62 years . Out of 20 eyes with pre operative intravitreal Bevacizumab , 15 patients (75%) had no bleeding, 3 (15%) were documented as mild and 2(10%) were documented ashaving severe post operative vitreous cavity bleed whrereas in the pre operative intravitreal Ranibizumab group out of 20 eyes , 16(80%) had no bleeding , 3(15%) had mild to moderate bleeding and 1(5%) were documented as severe post operative vitreous cavity bleeding in post operative followups.

Conclusion

Intravitreal Bevacizumab and Ranibizumab administered preoperatively to patients undergoing PPV for advance diabetic eye disease were found to be equally effective in minimizing post operative vitreous bleed in patients with ADED.

Keywords

Bevacizumab, Ranibizumab,vitreous hemorrhage, advanced diabetic eye disease, pars plana vitrectomy

INTRODUCTION:

Diabetic retinopathy is the most significant and the most common causes of visual impairment among the working age, that is 20-64 years old.Various studies have shown that at least 15.3-28.9% of patients with diabetes mellitus have some form of pre proliferative or proliferative diabetic retinopathy depending upon demographic factors as well as the duration of diabetes mellitus and degree of glycemic control.[2,3] Prevelance of advance diabetic eye disease have been found to be about 1.74% ranging from preproliferative to proliferative diabetic retinopathy .[4] According to ETDRS study , advance diabetic eye disease or ADED is defined as either a non-resolving vitreous hemorrhage and/or tractional retinal detachment(TRD) among diabetic patientshaving poor glycemic control.[5]The pathogenesis of ADED is linked to retinal ischemia and VEGF production which develops due to capillary endothelial damage resulting in capillary drop out along with microangiopathic changes that are mediated by disruptions in Virchow's triad along with development of advance glycation end products(AGEs) which mediate vascular endothelial cell damage mediated by reactive oxygen species and leads to the development and peoliferation of retinal neo-vascularization under the effect of VEGF(Vascular endothelial growth factor) .The endothelial linning of these neo vessels is leaky as the lack endothelial tight junctions and lead to development of leaky of dysfunctional blood retinal barrier leading to development of retinal edema. Intra-vitreal Avastin(Bevacizumab) which is an anti VEGF ,given preoperatively reduces the risk of post operative vitreous cavity bleeding after 23 gauge PPV for ADED.[7,8] Bevacizumab ,which is a monoclonal antibody which is an anatagonist at every isoforms of VEGF A receptor but mostly against VEGF 165 is a potent Anti VEGF which inhibits the formation of neo vessels that are leaky and friable with risk of bleeding and also reduce the leakage from existing neo vessels.

A recent study revealed that patients having advance diabetic eye disease either with vitreous cavity bleed or TRD ,who underwent 23 gauge PPV with preoperative intravitreal injection of bevacizumab(Avastin) 1.25mg/0.05ml, documented no vitreous cavity bleeding in 60.8%,mild bleed in 21.3% and severe bleeding only 17.9% that required per operative measures like intraocular diathermy.[11]

The purpose of our study is to compare the efficacy and effectiveness of pre operative intravitreal injection of Avastin (Anti VEGF) Vs intravitreal Ranibizumab (Patizra) before 23 gauge PPV in patients with ADED or to decrease and minimize the risk of post operative vitreous bleed following 23 PPV.

MATERIALS AND METHODS:

Our study was a quasi-experimental study, approved by our hospital ethical Review Board with a study period of six months approved before start of the study. This study was carried out in the Ophthalmology department, 2024
institute of Medical sciences/Services Hospital Lahore from January 2024 to june 2024. During this time period forty patients were selected with ADED for 23 gauge threePPV. Patients between the age of 30years to 65 years of age including male and female were part of the study with non-resolving vitreous hemorrhage, which is defined as vitreous bleed not resloving for 3 months post treatment with three first line intravitreal injections of Avastin(bevacizumab). Every patients in our inclusion criteria was explained verbally in detail and also explained in local language about the nature of this study , its objectives and its method along with selection criteria , patients who agreed to participate in this study were informed about the time and duration of follow-up visits of twelve weeks.All patients planned for 23 gauge three port PPV were divided into two groups,each of 20 eye each and 20 patients were injected with intravitreal injection Avastin (Bevacizumab) 1.25mg /0.05 ml, administered seven days before PPV and in the other group 20 patients were injected with intravitreal Ranibizumab(Patizra) 0.5 mg in 0.05 ml at least one week prior to the surgery .Injection Avastin and Patizra were administered with a 29 guage one cc syringe ,3.5mm from limbus and 4.0mm from limbus in pseuophakic and phakic patients respectively under topical anesthesia with procaine in the form of drops under aseptic sterile conditions in eye operation theatre.

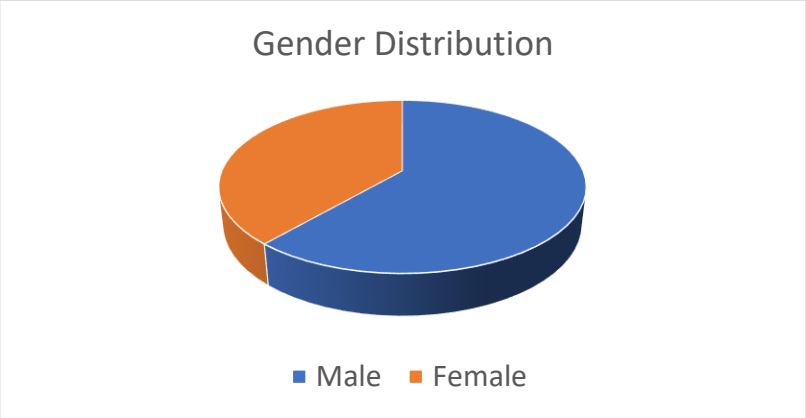
Following seven days of intravitreal injection Avastin(Bevacizumab) and Patizra (Ranibizumab), patients were operated for three PPV. A single surgeon performed all PPV procedures in our study using Millenium Vitrectomy Machine and 23 guage vitrectomy setup. The pars plana vitrectomy starts with insertion and securing three valved cannulas attached with sharp edge trocars, used for for primary scleral incision points points 3.5 mm behind the limbusin a pseudophakic eye and , 4 mm behind the surgical limbus in patients who are phakic , beacause of the biconvex shape of the crystalline lens. The infusion canula is attached to the inferotemporal entry port as it helps to maithain a constant tone of the eyeball throughout the surgical procedure and the flow into the eye ball via this canulla is secured via a suture tied at its attachment point with the trocar canulla to secure and place it firmly.To start the vitrectomy , core vitreous is removed along with any hemorrhage that clears the view for the rest of surgerical procedure, rest of vitreous is cleared by using triamcinolone to stain it due to its particulate nature that makes these vitreous strands visible , vitreous or posterior hyaloids face is stained and cleared followed by segmentation and delamination depending upon the type and extend of tractional retinal detachment .tractional retinal detachment needs either an en block disection or segmentation and delamination technique where as in case of adherent posterior vitreous cortex , posterior hyaliod detachment has to be performed at the optic disc margin .

Post operative data was collected by clinical examination of all patient who underwent PPV for ADED by slit lamp examination via 90D lens.A grading system for data record was used to measure the degree of post operative cavity bleed starting from mild, moderate and sever . Minimal bleeding or lack of any vitreous bleeding postoperatively was considered as evidence of effectiveness of Anti VEGF likeAvastin(Bevacizumab) and Patizra(Ranibizumab).

RESULTS:

Our study comprised of fourty patients out of which , twenty patients received a pre operative doze of intravitreal Avastin(Bevacizumab)1.25mg/0.05ml and the other 20 patients recieved intravitreal Patizra (Ranibizumab) , dose 0.5mg/0.05ml, one week prior to 23 gauge PPV.Out of total of fourty patients, 28(70%) were males and15 (30%) were females. Fig 1.

Figure 1



Patients had a mean age of 59.33±3.62 years (30-65 years). Duration of disease on average was 11.30±1.52 years.Out of 20 eyes with pre operative intravitreal Bevacizumab ,fifteen (75%) had no bleeding, three (15%) had mild and two(10%) recorded severe post operative vitreous bleed whrereas in the pre operative intravitreal Ranibizumab group among twenty eyes , sixteen (80%) had minimal bleeding , three (15%) had upto a level of moderate bleeding while one patient (5%) was graded as having severe post operative vitreous cavity bleed .

Table 1A Post operative hemorrhage grading

Intravitreal Drug	No bleeding	Graded as Mild	Graded as Severe
Bevacizumab (Avastin)	75%	15%	10%
Ranibizumab (Patizra)	80%	15%	5%

DISCUSSION :

A lot of recent evidence suggests clinical benefit of preoperative anti VEGF in patients with either vitreous cavity hemorrhage as well as tractional retinal detachment in terms of reduction in post operative cavity bleed as the Anti VEGF used preoperatively reduce the vascular component of the fibrvascular membranes and reduce capillary leakage as well .[20]Recent trials have made it clear that preoperative use of Anti VEGF is associated with a clear view of retina per operatively as compraed to the preoperative use of PRP laser , as the l;aser can be applied to a limited area due to vitreous hemorrhage.[21]Avastin has been shown to aid clearance of vitreous cavity bleed if used upyo ten days prior to planned PPV .[9]The preoperative Anti VEGF used , either Avastin or Patizra ,reduces the vascular components of firovascular proliferation and also reduce the proliferation of new vessels by counteracting VEGF produced in response to hypoxia of retinal tissue.[12]

In our study pre operative intravitrea lAvastin(bevacizumab) VS intravitreal Patizra(Ranibizumab) were injected seven days prior to PPV due to the fact that Bevacizumab and Ranibizumab both acts on 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 pruning as well as regression of the neo vessels sets in followed by the conversion of fibroblasts to myofibroblasts and leading to development of an inbalance between trans retinal vector forces that can lead to a worsening of tractional element or can cause the formation of a retinal break and lead to a combine traction and reghmatogenous retinal detachment .To avoid these complications to arise PPV must be done within seven days of intravitrealAvastin(Bevacizumab) and Patizra(Ranibizumab).

Patients with ADED that are undergoing PPV for tractional retinal detachment or resolving vitreous hemmorhage , have a high probability of post operative cavity bleed, as the neo vessels are leaky and the surgery induced transient inflamation makes the blood retinal barrier further weak transiently and thsi can precipitate post operati vitreous cavity hemorrhage .[14-19]
Results simillar to our study were produced with the use of intravitreal Bevacizumab (Avastin), with minimal post op bleed in fifty four percent of cases and mild to moderate bleeding in twenty seven percent of the patients after PPV .[7,22,13,18] Studies have shown that with the use of bevacizumab intravitrealy 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]

In conclusion, patients with ADED undergoing 23 gauge pars plana vitrectomy either for vitreous hemorrhage or tractional retinal detachment , can benefit from the pre operative intravitreal use of Bevacizumab and Ranibizumab as it minimizes the risk of post operative vitreous cavity bleed as well as post operative complications associated with post operative cavity hemorrhage.

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