

# Adjunctive Intravitreal Bevacizumab Injection at the End of Sutureless 23 G Vitrectomy for Diabetic Vitreous Hemorrhage

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## Abstract

This study aims to evaluate the safety and efficacy of intravitreal bevacizumab (IVB) at the end of vitrectomy in prevention of rebleeding in patients with diabetic vitreous hemorrhage.

**Methods:** This is a retrospective interventional study comprised of 30 eyes from 30 patients who underwent 23 G pars plana vitrectomy for diabetic vitreous hemorrhage (VH). IVB (1.25 mg/0.05 ml) was injected at the end of vitrectomy. Main outcome measure was the postoperative VH and reoperation 1 and 3 months of follow-up. Other outcome measures were Best-Corrected Visual Acuity (BCVA) and Intraocular Pressure (IOP).

**Results:** Early rebleeding within one month postoperatively occurred in 3.3%. The rate of early rebleeding was significantly reduced ( $p=0.002$ ). Late VH after 1 month occurred in 6.6%. BCVA at 1 and 3 ms postoperative significantly improved ( $p < 0.01$ ). There was no significant increase in the rate of reoperation ( $p=0.27$ ).

**Conclusion:** Adjunctive IVB injection at the end of vitrectomy for diabetic vitreous hemorrhage is safe and effective in reduction of early rebleeding.

**Keywords:** Vitrectomy; Diabetic retinopathy; Bevacizumab

## Materials and methods

This retrospective case series trial included 30 eyes of 30 patients suffered from diabetic vitreous hemorrhage with or without Tractional Retinal Detachment (TRD). This work was performed according to the declaration of Helsinki. All patients signed informed consent, particularly, the off-label use of the drug and its risks. The inclusion criterion was persistent vitreous hemorrhage for more than one month. The exclusion criteria were previous ocular surgery other than cataract surgery, previous bevacizumab injection, neovascular glaucoma and combined tractional-rhegmatogenous retinal detachment. Best-Corrected Visual Acuity (BCVA) converted log MAR, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement, fundus examination by indirect ophthalmoscope, and B-scan ultrasonography were done for all patients. Postoperative examinations were done at postoperative one week, one month and three months. The severity of pre- and postoperative vitreous hemorrhage (VH) was graded such as: mild (retinal vessels and disc were visible), moderate (retinal vessels or disc was invisible), and severe (the optic disc was invisible). Early rebleeding was defined as VH occurring within 1 month after the surgery and late postoperative VH was defined as VH occurring after 1 month and within 3 months of surgery. All surgeries were done by a single surgeon. Sclerotomies were made 3.5 mm posterior to the limbus with a 23G microvitrectomy blade and cannula. Infusion cannula was introduced. The infusion pressure was adjusted to as high as 20 mmHg using the OS3 vitrectomy system (Oertli, Switzerland). A core vitrectomy was done to remove the hemorrhage. Fibrovascular tissues were removed by membrane dissection, segmentation and delamination techniques. Peripheral vitreous cortex was removed by shaving under sclera depression. Endolaser photocoagulation was done up to the ora. SF6 gas was used as a tamponade after fluid gas exchange. Intravitreal injection of 1.25 mg (0.05 ml) bevacizumab (Avastin, Genentech, South San Francisco, CA) was done. The postoperative treatment included 0.3% gatifloxacin eye drops four times per day for 1 week and 1% prednisolone acetate eye drops four times per day that was usually tapered off over

## Introduction

The recurrent postoperative hemorrhage is considered one of the commonest postoperative complications for the pars plana vitrectomy for proliferative diabetic retinopathy and advanced diabetic eye disease. The recurrent postoperative rebleeding incidence ranges from 29 to 75%. Early rebleeding after pars plana vitrectomy may be caused by the remaining peripheral blood clots or the fibrovascular tissue ruminants. Anterior fibrovascular proliferation and the sclerotomies neovascularization are considered to be the sources of late hemorrhage [1]. Intravitreal Bevacizumab (IVB) decreases macular edema in diabetic retinopathy [2-5]. IVB injection reduced the neovascularization and bleeding in [6-9]. The IVB injection has been showed to be an effective adjunctive before vitrectomy for proliferative diabetic retinopathy [7-11]. The aim of this work is to evaluate the safety and efficacy of IVB injection at the end of vitrectomy for diabetic vitreous hemorrhage.

4 weeks. Patients were informed to remain face down for one week. Topical beta blocker and carbonic anhydrase inhibitors were prescribed when IOP was higher than 22 mmHg.

### Statistical analysis

SPSS software (version 14.0; SSPS Inc., Chicago, IL) was used for statistical analysis. For all statistical tests,  $p < 0.05$  was considered significant.

### Results

The age of the patients ranged between 34 and 65 years with a mean of  $52.25 \pm 8.7$  years. Three eyes (10%) showed retinal tears occurred during posterior manipulations, including membrane removal. They were managed by endolaser photocoagulation. Early rebleeding within one month after vitrectomy occurred in one eye (3.3%). The rate of early rebleeding was significantly reduced ( $p = 0.002$ ). It was resolved spontaneously within 3 weeks. Late postoperative VH more than 1 month after surgery occurred in two eyes (6.6%). All of the cases with late VH had severe VH. One eye resolved spontaneously within 2 weeks. However, one eye with late VH had a repeated vitrectomy within one month. No case of NVG or recurrent retinal detachment. The mean preoperative BCVA was  $1.78 \pm 0.29$  Log MAR (Log MAR ranged between 1.08 and 3.00), (HM - 0.075). Three eyes (10%) had BCVA of 0.05. Final best corrected visual acuity showed improvement in 28 cases (93.3%), no change in two eyes (6.6%). The mean final best corrected visual acuity reached  $0.9 \pm 0.4$  Log MAR (Log MAR ranged from 0.6 to 3.00) (HM - 0.25). This improvement of mean BCVA was highly significant ( $p = 0.001$ ). Eight eyes (26.6%) reached 0.25. Repeated measures showed insignificant IOP changes at postoperative one week, one and three months ( $p = 1.00$ ).

### Discussion

Bevacizumab reduces retinal neovascularization and rebusis in diabetic retinopathy [12, 13]. Preoperative bevacizumab reduced intraoperative bleeding. [12-14] TRD increased in 18% of eyes that injected with bevacizumab one month before vitrectomy [7]. TRD increased in 5.2% of eyes that injected with bevacizumab 13 days before vitrectomy [11]. IVB injection failed to prevent rebleeding as it washed out during vitrectomy [7, 16]. In this work rebleeding could be due to fibrovascular tissue remnants that bled during the operation. IVB decreases the VEGF, retinal and disc neovascularization [9, 10, 17, 22]. Bevacizumab blocked VEGF, nitric oxide and endothelin-1, causing short period of vasoconstriction which may be similar to vascular regression. Several studies proved that intravitreal injection of bevacizumab before vitrectomy reduces the bleeding that may occur during the operation [8, 14, 15]. On the other hand, one study proved that bevacizumab injection at the end of vitrectomy didn't reduce the incidence of the rebleeding in eyes underwent vitrectomy for the management of proliferative diabetic retinopathy [18]. Late rebleeding could be due to the shorter bevacizumab half life in the eye that underwent pars plana vitrectomy. The half-life of bevacizumab is considered shorter in vitrectomized eyes as it might be washed earlier [19-21]. In other studies, BCVA of the

preoperative IVB injection group did not improve in comparison with the control group [7, 16]. In this trial, postoperative BCVA showed significant improved from the preoperative BCVA. This work had several limitations such as; retrospective, not randomized, limited patients and the possible bias in selection. Prospective randomized work with large sample size is needed to prove the adjunctive role of intraoperative bevacizumab in vitrectomy for advanced diabetic eye disease. This work showed that injection of bevacizumab at the end of pars plana vitrectomy for diabetic vitreous hemorrhage is a safe and effective adjunctive tool in reduction of early rebleeding after vitrectomy.

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