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Group B: Animal receiving HTD (780/mg/kg/day) dissolved in 0.1ml of distilled water for the whole duration of pregnancy – low dose treated group.

ROLE OF ADJUNCTIVE USE OF INTRAVITREAL BEVACIZUMAB FOR SEVERE PROLIFERATIVE DIABETIC RETINOPATHY BEFORE VITRECTOMY

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ABSTRACT

The purpose of this work to assess the results and to determine the appropriate timing of pars plana vitrectomy after pretreatment with intravitreal Bevacizumab for proliferative diabetic retinopathy. This prospective study was conducted in Eye Unit I, Services Hospital/ SIMS Lahore for the duration of 6 months from October 2008-March 2009. Twenty one eyes of fifteen patients suffering from problem of proliferative diabetic retinopathy (PDR) were included in this study. These consisted of male as well as female patients with age range of 40-65 years. A written informed consent was obtained from all patients. All of them were completely evaluated in Eye OPD, Lahore. Fluorescein angiography was advised to every patient. An intravitreal injection of 1.25 mg / 0.05 ml was given with complete antiseptic technique, three days to two weeks prior to pars plana vitrectomy. Minimum bleeding during pars plana vitrectomy of fibrovascular membrane and less post-operative complications were observed. The complications were less in cases having intravitreal injection of bevacizumab before surgery for shorter duration as compared to longer period. Adjunctive use of intravitreal bevacizumab for severe proliferative diabetic retinopathy before pars plana vitrectomy is very effective. The appropriate timing of vitrectomy after intravitreal bevacizumab need to be further evaluated.

Keywords: *Bevacizumab; Pars Plana Vitrectomy; Proliferative diabetic retinopathy; Fibrovascular membrane.*

INTRODUCTION

Proliferative diabetic retinopathy (PDR) is one of the most important causes of blindness in adults[1]. To date, pars plana vitrectomy and Argon laser are predominant treatments for proliferative diabetic retinopathy[2], while the risk of complication is of special concern due to the bleeding[3] from fibrovascular membrane (FVM). Bevacizumab (Avastin Genetech Inc, South San Francisco, California, USA) is a humanized vascular endothelial growth factor (VEGF) antibody used for metastatic colorectal carcinoma[4]. Recent reports have described the application of Bevacizumab to treat ocular neovascular disorder including proliferative diabetic retinopathy.[5-8] Adjunctive use of intravitreal Bevacizumab for severe proliferative diabetic retinopathy before pars plana vitrectomy has also been reported.[5-6] However the preferable timing from the intravitreal injection to surgery has not been determined. Present study was planned to assess the role of this injection in the management of proliferative diabetic retinopathy and to see the effect of duration between injection and vitrectomy.

PATIENTS AND METHODS

This study was conducted in Eye Unit I, Services Hospital/ SIMS Lahore for a duration of six months from October 2008-March 2009. Total Twenty-one eyes with PDR were evaluated of fifteen patients who included both males and females.

All the patients underwent complete ophthalmological examination including record of visual acuity, IOP, slit-lamp bimicroscopic examination, indirect ophthalmoscopy and complete medical evaluation in out patient eye department.

Fluorescein angiography was carried out in every patient before intravitreal Avastin injection to rule out macular ischaemia. Selection criteria for intravitreal Avastin before pars plana vitrectomy was recurrent vitreous haemorrhage with no tractional retinal detachment, good macular perfusion on fluorescein angiography and minimum tractional clinical element on B-scan. Consent was taken from every patient after discussion about risk and advantage of intravitreal injection. Dose of Avastin was 1.25 mg/ 0.05 ml. Intravitreal injection was given 3 days to 14 days before vitrectomy. Any complication occurring during operation was the assessment parameter in the present study.

RESULTS

The injection was given 7-14 days ahead of surgery in seven eyes. While in 14 eyes, injection was given less than seven days before surgery. All patients

showed remarkable regression of new vessels in fibrovascular membranes, which necessitated minimum intra-operative haemostasis and achieved complete resolution of retinal tractions. Extensive fibrosis of fibrovascular membrane accompanied with strong adhesion to the retina was found in seven eyes, which received intravitreal Bevacizumab, seven to fourteen days ahead of the surgery whereas fourteen eyes having shorter administration time of Bevacizumab did not show firm adhesion of fibrovascular membrane to the retina and peeling of pre-retinal membrane was not difficult during pars plana vitrectomy (Table 1).

Table 1: *Clinical data of 21 cases of proliferative diabetic retinopathy.*

No	Operated Eye	Duration between Bevacizumab injection and surgery (Days)	Complications
1.	Right	05	No
2.	Right	06	No
3.	Right	14	Yes
4.	Left	10	Yes
5.	Left	06	No
6.	Right	03	No
7.	Right	04	No
8.	Left	13	Yes
9.	Left	12	Yes
10.	Left	05	No
11.	Right	06	No
12.	Right	03	No
13.	Right	13	Yes
14.	Right	06	No
15.	Right	11	Yes
16.	Right	05	No
17.	Left	06	No
18.	Left	03	No
19.	Right	09	Yes
20.	Right	06	No
21.	Right	06	No

DISCUSSION

Fourteen eyes of PDR were successfully treated with combination of pars plana vitrectomy and Bevacizumab intravitreal injection. It has been observed that during pars plana vitrectomy of proliferative diabetic retinopathy (PDR) there is severe bleeding which obscures the surgical field and prolongs the surgical time, resulting in an increased number of complications and difficulty in handling the situation. Avery *et al*[5] have demonstrated the efficacy of Bevacizumab for the treatment of PDR, which remarkably attenuates the activity of fibrovascular membrane at one week post-administration. Results of our study correlate with these findings. Our cases showed less bleeding in surgical excision of fibrovascular membrane in subjects operated three to six days after administration of intravitreal Avastin. Therefore, it provided good visibility to surgeon and reduced the risks of surgical complications. However the generation of strong adhesion between fibrovascular membrane and retina was observed, in those eyes in which Bevacizumab was administered 1-2 weeks before surgery. In these cases peeling of proliferative retinal membrane from retina was very difficult, and sometimes it was impossible to separate posterior hyhoid.

Since the cases that received intravitreal Bevacizumab 3-6 days before surgery did not show extensive fibrosis of fibrovascular membrane, shorter administration period of Bevacizumab (less than 7 days) may be preferable[9]. Further studies are required on this subject to determine the appropriate timings of vitrectomy after intravitreal Bevacizumab injection.

In **conclusion** an appropriate use of intravitreal Bevacizumab is effective as an adjunctive therapy prior to vitrectomy for severe proliferative diabetic retinopathy.

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