Original Article

Efficacy of the Intravitreal Bevicizumab in the Treatment of Vitreous Hemorrhage in Proliferative Diabetic Retinopathy

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Purpose: To determine the efficacy of bevicizumab in the treatment of vitreous hemorrhage in proliferative diabetic retinopathy.

Material and Method: The hundred patients with type I and type II diabetes mellitus for more than 7 to 8 years and having New vessels at the disc (NVD) or elsewhere on the fundus (NVE) were collected from Mayo hospital outpatient department. After taking informed consent and recording the demographic details including name, age, sex, address etc patients were admitted in ward of Eye unit I for injection bevicizumab (Avestin). Patients were evaluated and graded by directly taking the fundus picture and B-scan. Patients were examinned second week and finally on the fourth week by again directly taking the fundus photograph and doing the B – scan for assessing the efficacy of bevicizumab.

Results: Intravitreal Avastin reduced the vitreous hemorrhage in 39% of patients while in 61% of patients it was not successful in suppressing the vitreous hemorrhage.

Conclusion: Intravitreal Avastin reduced the chance of the vitreous hemorrhage and hence improved the vision and significantly prevented the patients from the massive surgical procedure of vitrectomy.

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Introduction

Diabetes is one of the most prevalent diseases in the world. About 171 million people suffer from the diabetes world wide, which is about 2.3% of the total population. The world diabetes is coined by Aretaeus of Cappadocia, which mean excessive urine. In 1675 the world mellitus was added by Thomas Willis which means honey as the urine was sweet. Blindness is one of the most feared complications of diabetes but also one preventable. Proliferative diabetic retinopathy and vitreous hemorrage is the commonest cause of blindness not only in Pakistan but also all over the world.[1.2] According to National Health Survey of Pakistan there are 4 – 8 million diabetics in the country Ten year incidence rate for vitreous hemorrhage is 40.1% in pati-

ents with type 1 diabetes mellitus and 29.9% in patients with type 2 diabetes mellitus.[2]

Vitreous hemorrhage is the common cause of sudden visual impairment in diabetic retinopathy usually results from the breakdown of blood vessel which leads to abnormal accumulation of blood in retinal layers and in-front of the retina.

Previously, the demonstrated means to reduce the risk of visual loss from vitreous hemorrhage was intensive glycemic control, conservative management of wait and see policy and in persistant cases vitrectomy was performed.

Recently, it was found that both intravitreal concentrations of interleukin – 6 (IL – 6), and vascular endothelial growth factor (VEGF), were increased in vitreous hemorrhage[5] and many reports indicated that Intravitreal injection of bevacizumab, a full – length humanized monoclonal anti-VEGF antibody, is effective in reducing the leakage of blood from the new vessels due to diffuse diabetic vitreous hemorrhage by preventing the rebleed.[6]

This study helped us in determining the efficacy of intravitreal Avastin in treating the patients with persistant vitreous hemorrhage so that we can have a simple, cost effective treatment with early results.

Material and Method

Hundred (100) patients were selected for study out of which 55 were males and 45 were females patients were selected from eye outpatient department in institute of ophthalmology mayo hospital Lahore. A written informed consent was taken from all the patients prior to treatment. Demographic profile of patient was obtained.

All patients were treated by single person. Proliferative diabetic retinopathy complicated with the vitreous hemorrhge was treated by 0.05 ml (1.25 mg) of intravitreal Avastin with 1 cc sterilized disposable syringe after instillation of topical anaesthetic drops.

All patients were sent home same day after a period of 1 hour observation. No complications (endophthalmitis and retinal detachment) after intravitreal Avastin was noted. All patients were asked for follow up 24 hours later. Patients were examined by 3 weeks and then 3 months and direct fundus picture were taken.

Inclusion Criteria

The patients included in study were *both* genders, Patients who provide the informed consent, Patients with vitreous hemorrhage, Patients with type I and II diabetes mellitus for more than 7 to 8 years and had proliferative diabetic retinopathy.

Exclusion Criteria

The Patients excluded had Aphakia, Media opacities that precluded the visualization of fundus by Slit lamp biomicroscope, Patient on systemic steroids, History of ischemic heart disease. Known allergy to the Components of the drug, tractional Retinal detachment or rhegmatogenous retinal detachment, and Patients with the history of known renal disease or with creatinine levels of more than 1.8.

Results

Hundred patients 55 males and 45 females age varies from 38 years to 65 years were selected randomly from the out patients department and they all had proliferative diabetic retinopathy complicated with the vitreous hemorrhage and the patients with grade iii and iv were selected and after confirming the diagnosis on slit lamp biomicroscope with 78 D, b scan and the fundus picture the patients were given the intravitreal Avastin and they were examined on the second and the fourth weeks to see the vitreous hemorrhage has cleared or not.

After taking the consent about the injection, Patients were dropped and given the local topical anesthesia and they were injected with the bevicizuma (Avestin) 4.0 mm from the limbus. They were kept under observation for an hour and then discharged. The patients were reexamined the very next day, about 3 weeks later and then after 3 months for the changes in the vitreous hemorrhage. Out of the hundred patients it was taken as the reference that if grade iii or grade iv is reduced to grade i or ii it will be considered significant. It was observed that 39 patients had the improvement in the clearance of vitreous hemorrhage and the 61 patients had no improvement in the vitreous hemorrhage.

Discussion

Diabetic retinopathy is a leading cause of blindness

and is commonly viewed as a vascular complication of diabetes mellitus. Diabetic retinopathy is a microangiopathy of the retina from which nearly all persons with diabetes eventually suffer. Diabetic retinopathy is subdivided into non-proliferative and proliferative retinopathy. The main risk factors for the development and progression of diabetic retinopathy are long duration of diabetes and poor control of blood sugar and arterial blood pressure.

Diabetic retinopathy complicated with vitreous hemorrhage is a manifestation of diabetic retinopathy and is the leading cause of blindness in diabetic patients. Although several treatment modalities are under investigation, the only demonstrated means to reduce the risk of vision loss as demonstrated by the ETDRS; intensive glycemic control, as demonstrated by the Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study; and blood pressure control, as demonstrated by the United Kingdom Prospective Diabetes Study. However, there has been interest in other treatment modalities, such as pharmacologic therapy with oral protein kinase C inhibitors and the use of intravitreal corticosteroids, because most laser – treated eyes do not exhibit satisfactory improvements in VA. Antibodies targeted to VEGF have also generated considerable interest and are being investigated.

VEGF is an endothelial cell-specific mitogen and angiogenic inducer in a variety of *in vitro* and *in vivo* models. It is upregulated by hypoxia, and it plays a role in vitrous hemorrhage and contributes to the in diabetic patients by controlling the formation of the new vessels. Bevacizumab is a full – length humanized monoclonal antibody that binds and inhibits all biologically active isoforms of VEGF. Although preclinical experimental data from primates suggested that the full – length antibody might not penetrate the internal limiting membrane of the retina, recent studies have shown full – thickness penetration of the retina within 24 hours. Recently, Spade.[7] published a prospective, noncomparative case series of patients with PDR treated with 1.25 mg bevacizumab. There was a significant reduction in vitreous hemorrhage at 2 weeks.

In the present investigation, we found that significant improvement in visual acuity that was achieved soon after intravitreal bevacizumab injection, and the beneficial effects lasted for 3 months. A study shows clearance of vitreous hemorrhage in about 39% of patients, three months after treatment with intravitreal Avastin in patients of diabetics complicated with vitreous hemoohage.

In our study, the results were almost consistent to the previously mentioned studies. i.e avastin is beneficial in suppressing the vitreous hemorrhage.

Conclusion

Our study concluded that up to three months after intravitreal Avastin in diabetic vitreous hemorrhage there is reduction in vitreous hemorrhage. However, long term effects of both the treatment modalities need to be studied.

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