Effectiveness of Intravitreal Bevacizumab (Avastin) Injection in Patients with Proliferative Diabetic Retinopathy

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Abstract

Background: Proliferative diabetic retinopathy (PDR) is a vision-threatening complication of diabetes mellitus. Intravitreal Bevacizumab (Avastin), an anti-VEGF agent, is widely used to regress retinal neovascularization.

Objective: To evaluate the effectiveness of intravitreal Bevacizumab injection among the patients with proliferative diabetic retinopathy.

Methods: This comparative cross-sectional study was conducted at the Department of Ophthalmology, Sheikh Fazilatunnesa Mujib Eye Hospital & Training Institute from July 2022 to December 2023. A total of 112 PDR patients were equally divided into controlled (n=56) and uncontrolled (n=56) diabetes groups. All patients received intravitreal Bevacizumab (1.25 mg) and were followed up at 1 day, 2 weeks, and 1 month. Treatment response was assessed by fundus fluorescein angiography and categorized as complete, partial, or no regression.

Results: The mean duration of diabetes mellitus was significantly higher among uncontrolled diabetic patients compared to controlled diabetic patients (15.4±4.36 vs. 10.8±3.98 years; p=0.001). IDDM was more common in both groups; however, the distribution of diabetes type was not significantly associated with glycemic control status (p=0.315). On the 1st post-procedure day, all patients in both groups showed no response to treatment. At the 2nd week follow-up, 96.4% of controlled diabetic patients achieved complete regression and 3.6% showed partial regression, whereas among uncontrolled diabetic patients, 32.1% achieved complete regression, 48.2% showed partial regression, and 19.6% showed no response (p=0.001). Similar findings were observed at the 4th week follow-up (p=0.001).

Conclusion: Intravitreal Bevacizumab (Avastin) injection was found to be effective in the treatment of proliferative diabetic retinopathy, particularly among patients with well-controlled diabetes mellitus.

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Introduction

Diabetes mellitus (DM) is one of the most important global public health challenges of the twenty-first century.[1] The worldwide prevalence of diabetes has increased substantially over recent decades, leading to a growing burden of chronic microvascular and macrovascular complications. Among these complications, diabetic retinopathy (DR) remains one of the leading causes of preventable visual impairment and blindness among working-age adults worldwide. DR develops as a consequence of prolonged hyperglycemia-induced damage to retinal microvasculature, resulting in increased vascular permeability, capillary occlusion, retinal ischemia, and neovascularization. The increasing prevalence of diabetes is expected to substantially increase the number of individuals affected by DR in the coming years, emphasizing the need for effective strategies for prevention and treatment.[1,2]

Recent global estimates indicate that approximately one-third of individuals with diabetes develop some degree of diabetic retinopathy, while a significant proportion progress to vision-threatening stages of the disease. The global burden of DR continues to rise, and projections suggest a considerable increase in affected individuals by 2045 due to population growth, aging, and increasing prevalence of diabetes.[2] Furthermore, diabetic retinopathy remains a major contributor to blindness and moderate-to-severe vision impairment worldwide, particularly in low- and middle-income countries where access to regular screening and specialized ophthalmic care may be limited.[3]

Diabetic retinopathy is generally classified into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). PDR represents the most advanced stage of the disease and is characterized by the formation of abnormal new blood vessels on the retinal surface and optic disc. These fragile neovessels can lead to vitreous hemorrhage, tractional retinal detachment, neovascular glaucoma, and severe irreversible vision loss. The pathogenesis of PDR is strongly linked to retinal ischemia and the upregulation of angiogenic factors, particularly vascular endothelial growth factor (VEGF). Elevated intraocular VEGF concentrations stimulate pathological neovascularization and increase vascular permeability, making VEGF a critical therapeutic target in the management of PDR.[4,5]

For several decades, panretinal photocoagulation (PRP) has been considered the standard treatment for proliferative diabetic retinopathy. PRP reduces retinal ischemia and decreases VEGF production, thereby inducing regression of neovascularization and reducing the risk of severe vision loss. However, laser treatment may be associated with adverse effects such as peripheral visual field loss, reduced night vision, exacerbation of macular edema, and patient discomfort. These limitations have encouraged the development of alternative and adjunctive treatment approaches targeting the underlying molecular mechanisms of the disease.[6]

The introduction of intravitreal anti-VEGF agents has transformed the management of retinal vascular disorders, including diabetic retinopathy. Bevacizumab (Avastin) is a recombinant humanized monoclonal antibody that binds to and inhibits all biologically active isoforms of VEGF. Although initially developed for systemic treatment of colorectal carcinoma, intravitreal Bevacizumab has been widely used off-label in ophthalmology because of its effectiveness, availability, and relatively low cost. By neutralizing VEGF activity, Bevacizumab promotes regression of

retinal neovascularization, reduces vascular leakage, and improves retinal oxygenation.[4,7]

Several studies have demonstrated the beneficial effects of intravitreal Bevacizumab in patients with proliferative diabetic retinopathy. Anti-VEGF therapy has been shown to induce rapid regression of neovascularization, reduce vitreous hemorrhage, facilitate vitrectomy, and improve retinal anatomical outcomes.[8,9] Furthermore, large clinical trials evaluating anti-VEGF agents have demonstrated that these treatments are at least comparable to conventional laser therapy in selected patients with PDR. Despite these promising outcomes, treatment responses may vary considerably among patients, suggesting the influence of systemic and ocular factors on therapeutic effectiveness.[10,11]

Glycemic control is one of the most important modifiable risk factors influencing the development and progression of diabetic retinopathy.[12] Persistent hyperglycemia contributes to retinal ischemia, oxidative stress, inflammation, and VEGF overexpression, all of which promote disease progression.[13] Previous epidemiological and clinical studies have consistently shown that poor glycemic control is associated with increased severity of diabetic retinopathy and a higher risk of progression to proliferative disease.[14,15] However, limited evidence is available regarding the extent to which glycemic control influences the response to intravitreal Bevacizumab treatment among patients with established proliferative diabetic retinopathy.

Understanding the relationship between diabetic control status and treatment outcomes may help clinicians identify patients who are more likely to benefit from anti-VEGF therapy and reinforce the importance of optimal metabolic control in the management of diabetic eye disease. Therefore, the present study was conducted to evaluate the effectiveness of intravitreal Bevacizumab (Avastin) injection in patients with proliferative diabetic retinopathy and to compare treatment outcomes between patients with controlled and uncontrolled diabetes mellitus.

Methods

This comparative cross-sectional study was conducted in the Department of Ophthalmology at Sheikh Fazilatunnesa Mujib Eye Hospital & Training Institute from July 2022 to December 2023. A total of 112 patients diagnosed with proliferative diabetic retinopathy (PDR) were enrolled in the study and equally divided into two groups: controlled diabetes mellitus (n=56) and uncontrolled diabetes mellitus (n=56).

Patients of either gender and any age with insulin-dependent diabetes mellitus (IDDM) or non-insulin-dependent diabetes mellitus (NIDDM) having proliferative diabetic retinopathy were included in the study irrespective of the duration and severity of diabetes. Patients with bleeding disorders, history of ocular surgery within the previous six months, active ocular infection, previous intravitreal Bevacizumab (Avastin) injection, recent myocardial infarction, uncontrolled hypertension, pregnancy, obesity, and smoking history were excluded from the study. Diabetes mellitus was considered controlled when random blood sugar was <14 mmol/L on medication and uncontrolled when random blood sugar was >14 mmol/L despite medication.

Baseline ophthalmic evaluation including fundus fluorescein angiography (FFA) was performed in all patients before treatment. Intravitreal injection of 1.25 mg Bevacizumab (Avastin) was administered 3.5 mm from the limbus into the vitreous cavity under topical

anesthesia using aseptic precautions. Patients were followed up on the 1st post-procedure day, at 2 weeks, and at 1 month after injection. Follow-up FFA was performed one month after the first injection to determine the final treatment outcome.

Effectiveness of intravitreal Bevacizumab was assessed by comparing pre- and post-treatment fluorescein angiographic findings of retinal neovascularization. Treatment response was categorized as complete regression when there was no leakage or only minimal staining of dye, partial regression when there was a definite reduction in dye leakage intensity, and no response when there was no change in leakage intensity. Both complete and partial regression was considered effective treatment outcomes.

Data were entered, cleaned, and analyzed using the Statistical Package for Social Sciences (SPSS), version 26 (IBM Corp., New York, USA). Descriptive statistics were expressed as frequency and percentage for categorical variables; as mean and standard deviation (SD) for continuous variables. The Chi-square test was used to assess associations between categorical variables. A p-value <0.05 at a 95% confidence level was considered statistically significant.

They were informed of their right to withdraw at any time without consequences, and confidentiality of all data was strictly maintained. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Sheikh Fazilatunnesa Mujib Eye Hospital & Training Institute, Gopalganj, Dhaka, Bangladesh.

Results

Table I shows the baseline characteristics of the study participants according to diabetic control status. The mean age of patients with controlled diabetes was 56.0 ± 11.1 years, while that of uncontrolled diabetes was 54.0 ± 10.8 years. The difference in age between the two groups was not statistically significant (p=0.062). However, the mean duration of diabetes mellitus was significantly higher among patients with uncontrolled diabetes (15.4 ± 4.36 years) compared to those with controlled diabetes (10.8 ± 3.98 years). This difference was statistically significant (p=0.001).

Table II shows the association between type of diabetes mellitus and glycemic control among patients with proliferative diabetic retinopathy. Among the controlled diabetes group, 89.3% patients had IDDM, while 10.7% had NIDDM. In the uncontrolled diabetes group, 82.1% had IDDM and 17.9% had NIDDM. Although IDDM was more common in both groups, the difference in the distribution of diabetes type between controlled and uncontrolled diabetic patients was not statistically significant (p=0.315).

Table III demonstrates the effects of intravitreal Bevacizumab treatment during post-procedure follow-up among patients with proliferative diabetic retinopathy according to glycemic control status. On the 1st post-procedure day (PPD), all patients in both the controlled and uncontrolled diabetes groups showed no response to treatment, and there was no statistically significant difference between the groups (p=1.000). However, by the 2nd week of follow-up, marked improvement was observed among patients with controlled diabetes. In this group, 96.4% of patients achieved total regression and only 3.6% showed partial regression, with no cases of non-response. In contrast, among uncontrolled diabetic patients, only 32.1% achieved total regression, 48.2% showed partial regression, and 19.6% had no response to treatment. This difference between the groups was statistically significant (p=0.001). Similar findings were observed at the 4th week

follow-up, where controlled diabetic patients maintained a significantly better treatment response compared to uncontrolled diabetic patients (p=0.001).

Table I: Baseline characteristics of the study participants (N=112)

Characteristics	Controlled diabetes (n=56)	Uncontrolled diabetes (n=56)	*p*-value
Age in years Mean ± SD	56.0 ± 11.1	54.0 ± 10.8	0.062
Duration of DM (in years) Mean ± SD	10.8 ± 3.98	15.4 ± 4.36	0.001

Independent samples t-test done; p value <0.05 was considered as a significant value

Table II: Association between type of DM with Proliferative Diabetic Retinopathy patients (N=112)

Type of DM	Controlled diabetes (n=56)	Uncontrolled diabetes (n=56)	*p*-value
	n (%)	n (%)	
IDDM	50 (89.3)	46 (82.1)	0.315
NIDDM	6 (10.7)	10 (17.9)	

Chi-square test done; p value <0.05 was considered as a significant value

Table III: Effects of treatment after post procedure follow-up (N=112)

Follow-up	Controlled diabetes (n=56)			Uncontrolled diabetes (n=56)			*p*-value
	Total regression	Partial regression	No response	Total regression	Partial regression	No response	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
1st PPD	0 (0)	0 (0)	56 (100)	0 (0)	0 (0)	56 (100)	1.000
2nd week	54 (96.4)	2 (3.6)	0 (0)	18 (32.1)	27 (48.2)	11 (19.6)	0.001
4th week	54 (96.4)	2 (3.6)	0 (0)	18 (32.1)	27 (48.2)	11 (19.6)	0.001

Chi-square test done; p value <0.05 was considered as a significant value

Discussion

The present study evaluated the effectiveness of intravitreal Bevacizumab (Avastin) injection in patients with proliferative diabetic retinopathy (PDR) and compared treatment outcomes according to glycemic control status. The findings demonstrated that intravitreal Bevacizumab effectively induced regression of retinal neovascularization, with significantly better outcomes observed among patients with controlled diabetes.

The mean age of the participants was comparable between the controlled and uncontrolled diabetes groups, indicating that age was unlikely to influence treatment outcomes. Similar age distributions have been reported in previous studies of patients with PDR receiving anti-VEGF therapy.[16,17] In contrast, the duration of diabetes was significantly longer among patients with uncontrolled diabetes, which is consistent with findings from the UK Prospective Diabetes Study (UKPDS) and other studies demonstrating that longer disease duration is associated with progression of diabetic retinopathy and poorer metabolic control.[10,18,19]

A key finding of this study was the significantly greater regression of retinal neovascularization among patients with controlled diabetes. At both the second and fourth weeks of follow-up, 96.4% of controlled diabetic patients achieved complete regression, compared with only 32.1% of uncontrolled diabetic patients. Furthermore, no treatment failure was observed in the controlled diabetes group, whereas 19.6% of uncontrolled diabetic patients showed no response. These findings suggest that glycemic control plays an important role in determining the effectiveness of anti-VEGF therapy.

The overall effectiveness of intravitreal Bevacizumab observed in this study is consistent with previous reports. Avery et al. and Arevalo et al. demonstrated rapid regression of retinal neovascularization following intravitreal Bevacizumab injection in patients with PDR.[7,20] Similarly, Osaadon et al. concluded that anti-VEGF agents are effective in suppressing VEGF-mediated angiogenesis and promoting regression of retinal neovascularization.[4]

The superior treatment outcomes among patients with controlled diabetes may be explained by the adverse effects of chronic hyperglycemia on retinal microvasculature. Persistent hyperglycemia promotes oxidative stress, inflammation, endothelial dysfunction, and increased VEGF expression, which contribute to ongoing retinal ischemia and neovascularization.[21] Landmark studies such as the DCCT and UKPDS demonstrated that intensive glycemic control significantly reduces the development and progression of diabetic retinopathy.[18,22] The findings of the present study extend this evidence by suggesting that good glycemic control may also enhance the response to intravitreal Bevacizumab therapy.

The study has several limitations, including its single-center design, relatively small sample size, short follow-up period, and the use of random blood glucose rather than HbA_1c to assess glycemic control. Nevertheless, the findings indicate that intravitreal Bevacizumab is an effective treatment for proliferative diabetic retinopathy and that optimal glycemic control is associated with significantly better therapeutic outcomes.

Conclusion

Intravitreal Bevacizumab injection was effective in inducing regression of retinal neovascularization in patients with proliferative diabetic retinopathy. Patients with well-controlled diabetes demonstrated significantly better treatment outcomes compared with those having uncontrolled diabetes. These findings highlight the importance of optimal glycemic control in enhancing the therapeutic response to intravitreal Bevacizumab in proliferative diabetic retinopathy.

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