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Original Article

Effectiveness of Intravitreal Bevacizumab (Avastin™) in Vitreous Hemorrhage Associated with Proliferative Diabetic Retinopathy

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ABSTRACT

Proliferative diabetic retinopathy (PDR) is a major cause of vision loss in diabetic patients. Vitreous haemorrhage (VH) is a common complication of PDR that significantly affects visual acuity. Intravitreal bevacizumab (Avastin™) has been used as a treatment option for VH associated with PDR. **Objectives:** To determine the effectiveness of intravitreal bevacizumab (Avastin™) in clearing vitreous haemorrhage and improving visual acuity in patients with PDR. **Methods:** This quasi-experimental study was conducted at the Ophthalmology Department, Hayatabad Medical Complex, Peshawar, from 01-01-2025 to 30-06-2025. A total of 79 patients with PDR-associated VH were included. Patients received three intravitreal bevacizumab injections at monthly intervals. Outcomes included VH clearance, improvement in best corrected visual acuity (BCVA), and requirement of pars plana vitrectomy. Data were analysed using SPSS version 22.0. Paired sample t-test and Chi-square test were applied, with $p \leq 0.05$ considered statistically significant. **Results:** The mean age of participants was 41.49 ± 10.54 years. VH clearance was observed in 67 (84.8%) patients, while improvement in BCVA occurred in 57 (72.2%) patients. Pars plana vitrectomy was required in 14 (17.7%) patients. Mean BCVA significantly improved from 0.81 ± 0.10 logMAR pre-therapy to 0.45 ± 0.24 logMAR post-therapy ($p<0.001$). Significant associations were observed between baseline BCVA and improvement in visual acuity ($p=0.011$) and requirement of vitrectomy ($p=0.046$). **Conclusions:** Intravitreal bevacizumab (Avastin™) is an effective treatment for VH in PDR, resulting in significant improvement in visual acuity, enhanced haemorrhage clearance, and reduced need for surgical intervention.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is the largest growing epidemic globally, with a reported recent prevalence of 10.5%, which approximates to half a billion people [1]. In Pakistan, this epidemic is also on the rise, making this country rank in the top ten nations that are sufferers of this potentially life-threatening condition, with a prevalence of 10%, approximating to a population of 24 million people [2]. This disease can impact the life of a sufferer since it can not only reduce the quality of life of patients but also cause a significant economic burden [3, 4]. One reason that can be attributed to this high economic burden, as well as the decline in quality of life, is the development of diabetic retinopathy (DR), which is among the leading causes of permanent blindness globally [5]. The primary mechanism by which this complication of T2DM develops is the production of abnormally high amounts of vascular endothelial growth factor (VEGF) in response to oxidative stress caused by persistently deranged glycaemic control. VEGF results in progressive proliferation of vessels in the retina, leading initially to non-proliferative and subsequently proliferative DR (PDR), which can result in intra-vitreal haemorrhage (VH) [6]. In these cases,

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Avastin™ (bevacizumab) is considered effective due to its anti-VEGF activity. Not only is this pharmacological agent believed to effectively clear the PDR-related VH, but it also prevents the development of VH in patients with PDR [7, 8]. In this instance, a study recently conducted reported that in patients who developed VH secondary to PDR, intravitreal bevacizumab (IVB) effectively cleared VH in 92% of the cases. Moreover, it was also found that IVB reduced the requirement of pars plana vitrectomy (PPV) by 72% and improved the best corrected visual acuity (BCVA) in 66% of the patients [9].

IVB can serve as a useful intervention in PDR and associated VH; however, supporting evidence in the local population is not only lacking but is also outdated. Furthermore, availability and cost are other factors that affect its usage in our community. This study was thus conducted to determine the effectiveness of IVB in the treatment of VH associated with underlying PDR. This study aimed to evaluate the effect of intravitreal bevacizumab in the treatment of vitreous hemorrhage in proliferative diabetic retinopathy.

METHODS

This quasi-experimental study was held at Hayatabad Medical Complex, Ophthalmology Department, Peshawar, Pakistan, from 1 January 2025 to 30 June 2025. Ethical approval was obtained from the Institutional Research & Ethical Board / Hospital Research and Ethical Committee (IREB), Hayatabad Medical Complex, Peshawar (Approval No. 939; dated 16th December 2022). The sample size was calculated for the estimation of a single proportion using the formula $n = Z^2 \times p(1-p)/ d^2$, where Z=1.96 for 95% confidence level, p=0.92 (anticipated frequency of vitreous haemorrhage clearance based on Wirkkala *et al.*), and d = 0.06 (margin of error) [9]. This yielded a minimum sample size of approximately 79 participants. The calculation was performed using the WHO sample size calculator/software. Before inclusion, it was ensured that all the parents of the patients gave their explicit informed consent in written form, for which a dedicated pre-printed form was used. Patients aged 25-60 years, male or female gender, who suffered from PDR and associated VH were included. Patients who previously used intravitreal Avastin™, had undergone pan-retinal photocoagulation (PRP) previously, pregnant women, had tractional or any other retinal detachment on B scan, which is a contraindication for intravitreal anti-VEGF injection, and those who had VH due to causes other than PDR (like retinal detachment, retinal vein blockage) were excluded. Diagnosis of PDR and associated VH was made through indirect fundoscopy showing dot and blot haemorrhages, hard exudates, and a network of abnormal new vessels on the retina, along with visualization of blood in the vitreous. Baseline characteristics, including age, gender, and BCVA, were documented. After that, all the included patients were treated with a course of three injections of bevacizumab in the vitreous that was given at one monthly interval under aseptic conditions. At the end of three months, patients were assessed for the effectiveness of bevacizumab. The primary measure of effectiveness was the frequency of clearance of VH. Secondary outcome measures of effectiveness were improvement in BCVA and the requirement of PPV in case VH was not cleared after therapy. Assessment of effectiveness outcomes was made after one week of completion of therapy.

All the collected data were input and analyzed with SPSS version 22.0. Qualitative and quantitative variables were collected using descriptive statistics. Qualitative variables (gender, clearance of VH, BCVA improvement, and requirement of PPV) were measured as frequency and percentage. Quantitative variables (age and BCVA) were measured as mean ± standard deviation (SD). VH clearance frequency stratification was based on age, gender, and pre-therapy BCVA. Post-stratification analysis was done using the chi-square test. A p-value≤0.05 was considered significant.

RESULTS

In this study, 79 patients were included. Mean age was 41.49 ± 10.54 years. There were 49 (62.00%) male and 30 (38.00%) female patients. Mean pre-therapy BCVA was 0.80 ± 0.10 logMAR (Table 1).

Table 1: Pre-therapy demographic characteristics of patients (n=79)

Characteristics	Mean ± SD / n (%)
Mean Age (years)	41.49 ± 10.54
< 42 years	45 (57.00%)
≥ 42 years	34 (43.00%)
Gender	
Male	49 (62.00)
Female	30 (38.00)
Mean BCVA (logMAR)	0.80 ± 0.10
< 0.9 logMAR	36 (45.60)
≥ 0.9 logMAR	43 (54.40)

SD = Standard deviation

The frequency of VH clearance in patients who were treated with intravitreal bevacizumab was 67 (84.80%). The frequency of improvement of BCVA post-therapy in these patients was 57 (72.20%). PPV was required in 14 (17.70%) patients. Stratification of effectiveness outcomes based on confounding variables, including age, gender, and pre-therapy BCVA (Table 2).

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Table 2: Stratification of Effectiveness Outcomes Based on Confounding Variables (n=79)

Outcomes	<42 years % (n=45)	≥42 years % (n=34)	p-value[c]
Age			
VH clearance	36	31	0.171
Improvement in BCVA	32	25	0.812
PPV Required	11	3	0.072
Outcomes	**Male % (n=49)**	**Female % (n=30)**	**p-value[c]**
Gender			
VH clearance	42	25	0.775
Improvement in BCVA	34	23	0.484
PPV Required	9	5	0.848
Outcomes	**<0.9 logMAR (n=36)**	**≥0.9 logMAR (n=43)**	**p-value[c]**
Pre-therapy BCVA			
VH clearance	33	34	0.120
Improvement in BCVA	31	26	0.011*
PPV required	3	11	0.046*

VH=Vitreous haemorrhage, BCVA=Best corrected visual acuity, PPV=Pars plana vitrectomy, c=Chi-square test
*indicates statistical significance at p≤0.050

A paired sample t-test was conducted to compare the best corrected visual acuity before and after intravitreal Bevacizumab injection. The mean pre-therapy BCVA was 0.81 ± 0.10 logMAR, which significantly improved to 0.45 ± 0.24 logMAR post-therapy. The mean improvement was 0.36 logMAR (95% CI: 0.30–0.41; t=13.16, df=78, p<0.001). These findings demonstrate that intravitreal Bevacizumab is highly effective in improving visual acuity in patients with vitreous hemorrhage due to proliferative diabetic retinopathy. This improvement corresponds approximately to a change from 6/38 to 6/17 vision, indicating a major functional gain (Table 3).

Table 3: Comparison of Pre-therapy and Post-therapy BCVA (logMAR) Using Paired t-Test (n = 79)

Variables	Mean ± SD	Mean Difference	95% CI of Difference	t-value	df	p-value
Pre-therapy BCVA	0.8089 ± 0.1002	–	–	–	–	–
Post-therapy BCVA	0.4519 ± 0.2380	0.35696 ± 0.24109	0.30296 to 0.41096	13.160	78	<0.001*

BCVA = Best corrected visual acuity,
* Indicates statistical significance at p ≤ 0.050

DISCUSSION

The present study focused on one of the therapeutic interventions of PDR, which is one of the prevailing ocular morbidities contributing to the high global burden of permanent visual loss [10]. In current study, focus was put on PDR cases further complicated by VH, which is a well-known complication of this diabetic complication of the retina [11, 12]. Therapeutic intervention in the present study was selected based on one of the most common pathophysiological mechanisms involved in the development of this condition, which is aberrant VEGF production mediated by neo-angiogenesis [13]. In the present study, the mean age of the patients suffering from PDR was 41.49 years. In comparison, a study found that the mean age of the patients suffering from this diabetic complication of the eye was 52 years, which is comparable to the present study [14]. In another study, in which clinical characteristics of patients with DR were analysed, it was found that the age range that was affected most by this diabetic complication was between 41 and 60 years [15]. This trend was also similar to the trend of age group distribution of this retinal disease in the present study, with more patients with this condition belonging to the older age group. One major reason that explains this trend is that as people grow older, their duration of having DM increases, which predisposes them to develop complications of this multi-system disease. Upon analysis of the distribution of this condition in genders, there was a clear male predominance observed in the present study, with males making up 62% of the study population. Similar to this trend observed in the present study, a study was conducted recently in Pakistani diabetic populations in which it was observed that among male patients, PDR was found in 25.2%, while in female patients, it was only found in 8.5%, exhibiting a clear male predominance [16]. In another study, similar male predominance was observed in the frequency distribution of DR among diabetic patients, with males making up the majority of patients having DR, reaching as high as 71.77% [17]. The exact mechanism of male predominance in this condition is not known, but according to previous literature, this difference is driven by multifactorial pathophysiology, including the gender differences in sex hormones, inflammatory cytokine profiles, and socio-behavioural aspects of life [18]. In the present study, the frequency of VH clearance in patients who were treated with intravitreal bevacizumab was 67 (84.80%). The frequency of improvement of BCVA post-therapy in these patients was 57 (72.20%). PPV was required in 14 (17.70%) patients. Compared to this, a study conducted in HD-treated patients with PDR-related VH with intravitreal bevacizumab. The results showed that VH was completely cleared in 92% of patients, and the BCVA was significantly improved compared to the pre-therapy

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BCVA in 66% of patients. In addition, they also reported that PPV was required in only 28% of the patients after this therapy [9]. Another study was conducted with a similar aim in Pakistan, in which 131 patients with concomitant VH and PDR were included. These patients were treated with the Avastin ™ therapy administered into the vitreous cavity at one-month intervals. After treatment, assessment was made in these patients, and it was found that only 33% patients exhibited no improvement in BCVA, while all other patients showed improved BCVA after therapy. Similarly, it was found that PPV was performed in 23.8% of the patients after administration of this useful therapy [19]. Similarly, in a comparative study, one group of PDR patients received bevacizumab therapy, and it was observed that the post-therapy BCVA was significantly improved as compared to the pre-therapy levels ($p < 0.001$), thereby exhibiting the effectiveness of this therapy in managing patients with PDR, which is a major vision-threatening diabetic complication [20]. The present study provides useful insights regarding the effectiveness of Avastin ™ therapy in managing patients with VH related to PDR. Its uniqueness lies in the fact that this study, instead of focusing on the PDR patients, focused on a specific subset of PDR patients who had VH, who often are managed surgically through PPV. Results from this study suggest that with the use of this intravitreal therapy, the rate of PPV can be reduced and VH can be managed effectively with favourable visual outcomes. Lack of control arm was the only limitation of the present study, for which the conductance of further clinical trials with a control arm in this specific subset of PDR patients is highly recommended.

Limitations of the study included that it was performed at a single tertiary care centre with a small sample size and a short duration of follow-up (three months). This study was also quasi-experimental and did not have a control or comparison group (laser photocoagulation or early vitrectomy). The outcome in terms of vitreous haemorrhage clearance and improvement in BCVA was observed without a detailed study of recurrence or long-term complications. We recommend conducting large multicenter randomized controlled trials with longer follow-up to evaluate sustained visual outcome, haemorrhage recurrence, and the need for later surgical intervention. Comparison with other modalities of treatment in proliferative diabetic retinopathy patients will add more strength to the present study.

CONCLUSIONS

In conclusion, intravitreal Avastin™ (bevacizumab) is a highly effective therapy in managing patients with proliferative diabetic retinopathy-related vitreous haemorrhage since it not only provides favourable outcomes in the form of clearance of vitreous haemorrhage and improvement in visual acuity but also reduces the need for surgical intervention in the form of pars plana vitrectomy.

Authors' Contribution

Conceptualization: Z
Methodology: Z
Formal analysis: Z, SI, MKK
Writing and Drafting: Z
Review and Editing: Z, SI, MKK, MIU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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