

Intravitreal Bevacizumab (Avastin) in Treatment of Vitreous Hemorrhage due to Proliferative Diabetic Retinopathy

Attaullah Shah Bukhari, Aijaz Ahmed Shah, Shahid Jamal Siddiqui

ABSTRACT

OBJECTIVE: To evaluate the role of intravitreal bevacizumab (Avastin) in treatment of vitreous hemorrhage due to proliferative diabetic retinopathy.

METHODS: This quasi-experimental trial was conducted at department of Ophthalmology Khairpur Medical College, Khairpur Mir's from January 2016 to June 2016. A number of 30 eyes of 30 patients having vitreous hemorrhage were selected and given intravitreal injection of bevacizumab 1.25 mg/0.05ml. Main outcome improvement in visual acuity with Snellen chart was observed at one week, four week and three months.

RESULTS: Among 30 eyes visual acuity improved in 4 eyes (13.33%) in 1st week, 24 eyes 80%, improve within four weeks, at the end of 3 months 25(83.33%) eyes improve in visual acuity, while 5 eyes (16.66%) developed recurrent vitreous hemorrhage.

CONCLUSION: In our study the Intravitreal bevacizumab produced partial or complete resolution of vitreous hemorrhage due to Proliferative Diabetic Retinopathy. Which is more useful in recent onset of hemorrhage. It is my suggestion that it can be a fine alternative of surgery.

KEY WORDS: Bevacizumab intravitreal injection, Vitreous hemorrhage, Proliferative Diabetic Retinopathy.

This article may be cited as: Bukhari AS, Shah AA, Siddiqui SJ. Intravitreal Bevacizumab (Avastin) in Treatment of Vitreous Hemorrhage due to Proliferative Diabetic Retinopathy. J Liaquat Uni Med Health Sci. 2018;17(02):76-9. doi: 10.22442/jlumhs.181720554

INTRODUCTION

Among all eye related disease, diabetic retinopathy (DR) is the leading cause of loss of vision in young adults^{1,2}. In Proliferative Diabetic Retinopathy (PDR), several angiogenic factors, like Vascular Endothelial Growth Factors cause neo-vascularization^{3,4}, fibro-vascular proliferation, vitreous hemorrhage & retinal detachment⁵. Vitreous hemorrhage is the most common ailment of proliferative diabetic retinopathy and one of the main cause of blindness⁶. Among diabetics, intraocular surgery⁷ causes increase in number of angiogenic factor like vascular endothelial growth factor, resulted due to surgical trauma and edema. Laser photo-coagulation is treatment of retinopathy in diabetics but it can be problematic in cases of cataracts or vitreous hemorrhage. Bevacizumab (Avastin, Genentech) is a humanized recombinant antibody, which joins all iso-forms of Vascular Endothelial Growth Factors. In 2006, Spade & Fisher explained the application of intravitreal bevacizumab for vitreous hemorrhage in Proliferative Diabetic Retinopathy patients, observing a decrease in neo-vascularization and vitreous hemorrhage was resolved. Visual acuity was improved from 2 to 5 lines

within a month. The purpose of this study was to evaluate the role of injection Bevacizumab (Avastin) in the treatment of vitreous hemorrhage due to proliferative diabetic retinopathy.

METHODOLOGY

This quasi-experimental trial was conducted on 30 patients with Proliferative Diabetic Retinopathy (PDR), who presented with VH (Vitreous Hemorrhage) were registered at the Ophthalmology Department, Khairpur Medical College, Khairpur hospital from January 2016 to June 2016. All patients were selected through non-probability purposive sampling. Study was approved by college ethical committee, informed written consent was taken from patients. The inclusion criteria was vitreous hemorrhage with decrease vision. The exclusion criteria was mature cataract, glaucoma and cardiac patients. After the detailed history complete physical and ocular examination was performed which included slit lamp examination, intraocular pressure, funduscopy and ocular B-scan before giving intraocular injection of bevacizumab topical moxifloxacin with tobramycin was given topically for prophylactic purpose. The intravitreal injection of bevacizumab 1.25mg/0.05ml was given under topical

anesthesia in the operation theater where the full antiseptic protocol was observed during procedure including povidone iodine and drapping⁸. The intraocular injection was given at inferotemporal side of the eye ball about 3.5 to 4mm away from limbus. After the injection patients were advised to use topical moxifloxacin and tobramycin eye drops four times a day for one week and were told to come for follow-up after one week, two weeks, three weeks, four weeks and then every month upto six months. During follow-up complete ocular examination was done including visual acuity, slit lamp examination, intraocular pressure and funduscopy. Injection was repeated after one month upto three months or more in cases where there was no improvement. In those cases where there was improvement of visual acuity and clearance of vitreous hemorrhage pan retinal photocoagulation was performed with argon laser. In cases of non-resolving vitreous hemorrhage the patients were referred to vitreoretinal surgeon for vitrectomy and endo laser. SPSS version 21 was used to analyze the data. Descriptive statistics was calculated and improvement in patient was presented as frequency and percentage.

RESULTS

Thirty eyes of thirty patients were evaluated, male were 20(66.66%) and female 10(33.33%). The mean age of patients was 57.2 ±9.2 years. Vitreous hemorrhage scaling is shown in table I. VHS grade 2 was observed in 14 (46.7%) eyes while VHS grade 3 was observed in 16 (53.3%) eyes (Table II). At baseline, 13 (43.3%) patients had CF, 15 (50%) had HM while 6.7% cases had PL +ve. After 1 week of injection, 10 patients improved from CF and HM to 6/36 or 6/60. After 4 weeks, only 2 (6.7%) patient had HM VA, which remained same after 3months. Table III shows the summary of visual acuity before and after injection. While 5 patients with recurrent vitreous hemorrhage were referred for vitrectomy (Table IV).

TABLE I: VITREOUS HEMORRHAGE SCALING (DRVS)

0	No VH
1	Mild VH with visible fundus details
2	Moderate VH with no visible fundus details but with orange fundus reflex.
3	Severe VH with no retinal details and noorange fundus reflex.

VH =Vitreous Hemorrhage.

TABLE II: BASELINE CHARACTERISTICS OF STUDY EYES (n=30)

Gender	
Male	20 (66.66%)
Female	10 (33.33%)
Age(yrs)	57.2 ±9.2 (range=40-75)
Inter2val b/w VH and IVB (weeks)	2 ±2 (range=2-4)
VHS	
2	14 (46.7%)
3	16 (53.3%)

VHS=Vitreous Hemorrhage Scale

TABLE III: SUMMERY OF VISUAL ACUITY BEFORE AND AFTER INJECTION

VHS	VA before Inj	VA after 1 week	VA after 4 week	VA after 3 months
2	CF2Meter	6/60	6/24	6/18
3	HM	HM	6/60	6/24
3	HM	HM	5/60	5/60 Referred for VR surgery
2	CF2meter	6/36	6/12	6/12
3	HM	CF2F	6/36	6/18
2	CF2meter	6/60	6/24	6/9
3	PL +ve	HM	6/60	6/60
3	HM	HM	6/36	6/36
2	CF2Feet	6/60	6/18	6/18
2	HM	HM	HM	HM Referred for VR surgery
3	HM	CF2F	6/36	6/24
2	CF2Feet	CF2F	6/24	6/12
3	HM	HM	6/36	6/18
2	CF	HM	6/24	6/9
3	HM	CF2F	6/36	6/24
2	CF2F	6/60	6/24	6/18
2	CF2F	6/60	6/24	6/12
3	HM	6/60	6/24	6/24
3	HM	HM	5/60	6/36
2	CF2F	6/36	6/12	6/12
3	HM	CF2F	6/36	6/18

2	CF2F	6/60	6/24	6/9
3	PL +ve	HM	6/60	6/60 Referred for VR surgery
3	HM	HM	3/36	6/24
2	CF2F	6/60	6/18	6/18
3	HM	HM	HM	HM Referred for VR surgery
2	CF2F	CF3F	6/24	6/12
3	HM	HM	6/60	6/60 Referred for VR surgery
2	CF2F	CF2F	6/24	6/9
3	HM	CF3F	6/36	6/24

VHS=Vitreous Hemorrhage Scale, PL= Perception of light, HM=Hand Movement, CF= Counting finger, F= Feet

TABLE IV: FOLLOW-UP OF PATIENTS AFTER TREATMENT (n=30)

VA		Frequency	Percent
Before injection	CF	13	43.3%
	HM	15	50.0%
	PL +ve	2	6.7%
After 1 week	6/36	2	6.7%
	6/60	8	26.7%
	CF	8	26.7%
	HM	12	40.0%
After 4 week	3/36	1	3.3%
	5/60	2	6.7%
	6/12	2	6.7%
	6/18	2	6.7%
	6/24	10	33.3%
	6/36	7	23.3%
	6/60	4	13.3%
	HM	2	6.7%
After 3 months	5/60	1	3.3%
	6/9	4	13.3%
	6/12	5	16.7%
	6/18	7	23.3%
	6/24	6	20.0%
	6/36	2	6.7%
	6/60	3	10.0%
	HM	2	6.7%
Referred for VR surgery		5	16.7%

DISCUSSION

Among all causes of vitreous hemorrhage, Proliferative Diabetic Retinopathy is the major cause. This ultimately results in blindness that can effect adult population. Until now pars plana vitrectomy was the only choice of treating vitreous hemorrhage. Scientists investigated the role of Intravitreal bevacizumab injection to treat vitreous hemorrhage. Repeated injections can be safe and effective. Memon AF et al⁹ in a study of intravitreal bevacizumab applied for post-vitrectomy diabetic vitreous hemorrhage, intravitreal bevacizumab was found to be quite effective in averting vitreous hemorrhage. Another study at LRBT eye hospital korangi Karachi by Sultan Z et al¹⁰ injection Avastin was given one week before micro incision vitrectomy surgery in diabetic vitreous hemorrhage patient and was proved fruitful. Study conducted by Sinawat S et al¹¹ injection Avastin is useful in new dense vitreous hemorrhage after PRP (pan retinal photocoagulation). Another study conducted by Yang CS¹², in taipai veterans' general hospital Taiwan in eye department injection Avastin given and PRP done in diabetic patient was very successful. A study conducted by Simumovic MP et al¹³ that use of Avastin or Ranibizumab and Pegaptanib in complicated proliferative diabetic retinopathy before parsplana vitrectomy decreases iatrogenic effects of surgery and gives superior functional and structural results at three to four months follow-up. Study conducted by Arevalo¹⁴ et al injection Avastin decreases retinal neovascularization in patients with proliferative diabetic retinopathy. A study conducted by Parikh R N¹⁵ et al proved that in proportion cases of vitreous hemorrhage after diabetic retinopathy, even one to two injection of Avastin could be sufficient. Study conducted by Uhumwangho OM¹⁶ in tertiary hospital of benin city of Nigeria, intravitreal Anti VEGF (Vascular Endothelial Growth Factor) Bevacizumab and Ranibizumab were very useful in treatment of many retinal vascular diseases like vitreous hemorrhage after diabetic retinopathy or macular edema or central retinal vein occlusion. Kumar A, et al¹⁷ state that injection Avastin has same effect as another Anti VEGF used in retinal vascular diseases but injection Avastin was cheaper and reducing economic burden.

CONCLUSION

In our study the Intravitreal bevacizumab produced partial or complete resolution of vitreous hemorrhage due to Proliferative Diabetic Retinopathy. Which is more useful in recent onset of hemorrhage. It is suggested that injection Avastin is fine alternative of vitrectomy surgery.

REFERENCE

1. Klein BE. Overview of epidemiologic studies of diabetic retinopathy. *Ophthalmic Epidemiol* 2007; 14(4):179–83.
2. Pascolini D, Mariotti SP. Global estimates of visual impairment. *Br J Ophthalmol* 2012; 96(5):614–8. doi: 10.1136/bjophthalmol-2011-300539
3. Lopes de Jesus CC, Atallah AN, Valente O, Moca Trevisani VF. Pentoxifylline for diabetic retinopathy. *Cochrane Database Syst Rev* 2008; 16(2):CD006693. doi: 10.1002/14651858.CD006693.pub2.
4. Mohamed QA, Ross A, Chu CJ. Diabetic retinopathy (treatment). *BMJ Clin Evid (Online)* 2011; pii: 0702.
5. Salam A, Mathew R, Sivaprasad S. Treatment of proliferative diabetic retinopathy with anti-VEGF agents. *Acta Ophthalmol* 2011; 89(5):405-11. doi: 10.1111/j.1755-3768.2010.02079.x
6. Sharma R, Joshi SN, Shrestha JK. Etiology of vitreous hemorrhage in a tertiary eye care center in Nepal. *Nepal J Ophthalmol* 2010; 2(2):121-6.
7. Patel JI, Hykin PG, Cree IA. Diabetic cataract removal: postoperative progression of maculopathy-growth factor and clinical analysis. *Br J Ophthalmol* 2006; 90(6):697–701.
8. McCannel CA, Flynn HW, Cunningham Jr ET. Updated Guidelines for Intravitreal Injection. *Rev Ophthalmol* 2015; 22(7):52-5.
9. Memon AF, ur-Rehman A, Shaikh FF. Intravitreal bevacizumab (Avastin) for post-vitreotomy diabetic vitreous hemorrhage. *Pak J Med Sci* 2011; 27(5): 1164-8.
10. Sultan Z, Rizvi SF, Qureshi FM, Mahmood SA. Role of bevacizumab in the prevention of early postoperative haemorrhage after 25-gauge microincision vitrectomy surgery. *Pak J Med Sci*. 2016; 32(5):1184-87.
11. Sinawat S, Rattanapakorn T, Sanguansak T, Yospaiboon Y, Sinawat S. Intravitreal bevacizumab for proliferative diabetic retinopathy with new dense vitreous hemorrhage after full panretinal photocoagulation. *Eye (Lond)*. 2013; 27(12):1391–96.
12. Yang CS, Hung KC, Huang YM, Hsu WM. Intravitreal bevacizumab (Avastin) and panretinal photocoagulation in the treatment of high-risk proliferative diabetic retinopathy. *J Ocul Pharmacol Ther*. 2013; 29(6):550–55.
13. Simunovic MP, Maberley DA. Anti-vascular endothelial growth factor therapy for proliferative diabetic retinopathy: A Systematic Review and Meta-Analysis. *Retina*. 2015; 35(10):1931–42.
14. Arevalo JF, Lasave AF, Wu L, et al. Intravitreal bevacizumab for proliferative diabetic retinopathy: results from the Pan-American Collaborative Retina Study Group (PACORES) at 24 months of follow-up. *Retina*. 2017; 37(2):334–43.
15. Parikh R N, Traband A, Kolomeyer AM, et al. Intravitreal Bevacizumab for the Treatment of Vitreous Hemorrhage due to Proliferative Diabetic Retinopathy. *Am J Ophthalmol* 2017; 176:194-202.
16. Uhumwangho OM. Indications and treatment outcomes of intravitreal bevacizumab and ranibizumab for retinal diseases in Benin City, Nigeria. *Niger J Ophthalmol* 2017; 25(1):14-7.
17. Kumar A, Ravani R. Using intravitreal bevacizumab (Avastin®) – Indian Scenario. *Ind J Ophthalmol* 2017; 65(7):545-8.



AUTHOR AFFILIATION:

Dr. Attaullah Shah Bukhari (*Corresponding Author*)

Assistant Professor, Department of Ophthalmology
Khairpur Medical College Khairpur Mir's, Sindh-Pakistan.
Email: drattaullahbukhari@yahoo.com

Dr. Aijaz Ahmed Shah

Assistant Professor, Department of Radiology
Khairpur Medical College Khairpur Mir's, Sindh-Pakistan.

Prof. Shahid Jamal Siddiqui

Department of Ophthalmology
Khairpur Medical College Khairpur Mir's, Sindh-Pakistan.